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BUREAU OF HYGIENE AND TROPICAL DISEASES.

TROPICAL DISEASES BULLETIN.

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CONTROL OF SCHISTOSOMIASIS.

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Any approach to the problem of schistosomiasis control, whether it be an investigation or some more direct attempt to reduce the incidence of the disease, will naturally be made from the standpoint of one or both of the main principles—prevention and treatment. Preventive methods in schistosomiasis are concerned with some phase in the rather complicated but well-known life-cycle of the parasite, and their efficacy and expediency are determined by factors which may vary with local exigencies of topography and custom. Treatment in schistosomiasis, which in this instance obviously implies mass treatment, involves the use of drugs; experience has shown that certain derivatives of antimony are the only effective, if not highly efficient, curative agents.

Prevention.

In recent years a considerable amount of research has been carried out, and field trials have been attempted in several regions to control schistosomiasis by the preventive method, with varying degrees of success. A general account of these is presented here under three headings: 1. Protection of snail-bearing waters from fouling and infection. 2. Destruction or reduction of snail populations. 3. Avoidance of cercarial infection.

1. *Protection of snail habitats from infection.*—The means for achieving this very desirable objective and thus breaking the bilharzia life-cycle at its outset may not always be to hand, nor easily applied, but the advantages of this form of control are manifold, whether it be achieved by education and propaganda or by some more directly practical measures. Considerable success in this direction appears to have attended the efforts of the Sudan Medical Service [Report of the Sudan Medical Service for the year 1936 (this *Bulletin*, 1938, v. 35, 266)]. Sanitary measures were employed, which comprised the placing of all villages at least 300 metres from snail-infested canals which in addition were fenced, and the provision of good wells and latrines near the villages. These measures, combined with treatment, have resulted in substantial reductions in the schistosomiasis incidence in parts of the Northern Province, in the Wadi Halfa District and in the Blue Nile Province.

2. *Destruction of snails.*—The most obvious, and usually the most practicable, method of breaking the bilharzia life-cycle is to kill or get rid of the snail intermediaries; and since the researches and recommendations of Leiper in Egypt [this *Bulletin*, 1915, v. 6, 437] opened up this field of attack in 1915,

most of the anti-bilharzia campaigns in subsequent years have been based on this principle.

The methods of snail control in operation or suggested in endemic areas are mainly as follows: the introduction of chemical or organic poisons into snail habitats; the removal of snails by manual labour; the removal of vegetation and other necessary elements in their environment; biological control by the introduction or encouragement of natural enemies or unsuitable types of vegetation; the reconstruction of natural watercourses (*e.g.* by canalization, cementing or covering); flushing, draining and drying of watercourses, and the removal of unnecessary bodies of water.

The most widely-used chemicals for snail destruction are copper sulphate, copper carbonate, slaked lime and ammonium sulphate. KHALIL and AZIM [this *Bulletin*, 1938, v. 35, 667] used copper sulphate in a concentration of 5 parts per million for 5 days in the streams and channels of the Dakhla Oasis, Egypt, and found it effective. BAUGÉ [this *Bulletin*, 1942, v. 39, 768] also obtained good results in Southern Tunisia with copper sulphate in a focus of *S. haematobium*. This salt has the disadvantage of rendering water unfit for human consumption for a while, but in Southern Rhodesia, MOZLEY [this *Bulletin*, 1942, v. 39, 11] found that malachite (mineralized basic copper carbonate) is just as effective, and less toxic; on the other hand it is more expensive, and less soluble. The system of control employed in Fayoum Province [BARLOW and AZIM, this *Bulletin*, 1945, v. 42, 1017] combines copper sulphate treatment of the larger canals with manual clearance of snails and vegetation from the lesser water-courses. The concentration of copper sulphate varies from 15 to 50 parts per million according to the amount of silt and vegetation present. At Oran in Algeria, a new focus of urinary schistosomiasis appeared after the initiation of an irrigation system, which created an immense habitat favourable for snails [ALCAY, MARILL and MUSSO, this *Bulletin*, 1943, v. 40, 467]. It was suggested that these canals be controlled by emptying and cleaning; but it is pointed out that it would be a measure of only temporary value, since the canals become restocked with snails from some natural source which should be found and controlled. [The dangers of "man-made" snail habitats of another kind have been indicated by MOZLEY (this *Bulletin*, 1945, v. 42, 516) in Southern Rhodesia, where small artificial pools polluted with human dejecta and litter become more heavily stocked with snails than are natural waters.]

In Venezuela, LUTTERMOSER [this *Bulletin*, 1943, v. 40, 849] records the successful control of *Planorbis* (*Australorbis*) *glabratus*, vector of *S. mansoni*, by the application of recently slaked lime to the waterways. He found that a 0·1 per cent. solution kills snails and eggs in a day or less. In field practice several treatments of canals, cement tanks and ½ kilometre of a river, kept the water free of snails for 6 months, but one treatment every 3 months was usually sufficient. Lime has the advantage also of being non-toxic to domestic animals and cultivated land, and possesses a useful anti-bacterial and cercaricidal action. JANSEN [this *Bulletin*, 1945, v. 42, 1018] also tested the effect of slaked lime in Catende, Pernambuco, against *Planorbis* (*A.*) *centrimetralis*, and obtained 100 per cent. snail mortality with a strength of 4–5 parts per thousand after 24 hours. The use of lime is deprecated by MOZLEY [this *Bulletin*, 1945, v. 42, 516] in Southern Rhodesia, since by increasing the lime availability it may encourage snail development in lime-deficient areas. He considers that quicklime is ineffective against bilharzia snails as a result of his experience in treating a small stream containing *Physopsis* and *Biomphalaria*.

Doubts about the efficacy of drying as a means of snail control have been raised by several workers. BRUMPT [this *Bulletin*, 1942, v. 39, 866] states that *Planorbis* (*A.*) *glabratus* has considerable resistance to drying, and that alter-

nate drying and filling of canals every 15 days is not effective. In laboratory experiments this species survived 50 days of drying more severe than would occur in nature. According to BARLOW and AZIM [this *Bulletin*, 1945, v. 42, 1017] *Bulinus truncatus* is not killed by emptying and drying canals for 40 days, and in laboratory tests this species revived after 12 months', and *Planorbis boissyi* after 10 months' desiccation in mud.

The amphibious intermediary of *S. japonicum*, *Blanfordia* (*Oncomelania*) *nosophora*, requires a somewhat different method of attack. MIYAJIMA [this *Bulletin*, 1939, v. 36, 623] describes the control of this species, which lives partly in the water of ditches and partly on their muddy and weedy margins, by applications of quicklime to the water in a strength of 1 per cent. for 10 hours, while snails outside the water are killed by a steam jet. Control measures against *S. japonicum* must take into account the fact that it is harboured by other definitive hosts as well as man. WU [this *Bulletin*, 1941, v. 38, 43] found the following animals naturally infected in China: sheep, goats, house-rats, dogs, cats, oxen, buffaloes and horses.

Biological control of snails by means of natural enemies such as ducks, hedgehogs and fish is undoubtedly valuable, but is practicable in only a limited range of circumstances. A case for bilharzia control by fish in South Africa and Rhodesia has been stated by CAWSTON [this *Bulletin*, 1937, v. 34, 797]. Biological control by means of aquatic plants such as *Pistia stratiotes* has been suggested by MOZLEY [this *Bulletin*, 1940, v. 37, 483] who noted that in Zanzibar and Tanganyika Territory snails are scanty in water whose surface is completely covered by aquatic or semi-aquatic plants. Biological control by planting *Balanites* trees along snail-infested watercourses has also been suggested. ARCHIBALD [this *Bulletin*, 1934, v. 31, 114] found that the fruit of this tree (*B. aegyptiaca* in Tropical Africa, Arabia, Egypt and Palestine), if treated in a certain way, produces a poison which is highly fatal to snails; and WAGER [this *Bulletin*, 1936, v. 33, 557] noted that the fruit of the South African species, *B. maughami*, has similar properties. It is also very toxic to other forms of aquatic life such as tadpoles, frogs, fish, etc., and its value as a snail-killer may, therefore, be offset by the danger of upsetting the balance of life in natural waters.

3. *Avoidance of cercarial infection.*—Individual prophylaxis is theoretically simple and consists merely in avoiding skin-contact with, or the drinking of, infected water, but this doctrine implies that persons liable to exposure are aware of the life-cycle of the parasite and may be nullified by the requirements of agricultural practice in some countries. BRACKETT [this *Bulletin*, 1940, v. 37, 149] showed experimentally that the cercariae responsible for schistosome dermatitis penetrate skin mainly when water is evaporating from it, so that vigorous wiping after bathing is a useful prophylaxis. The well-known fact that schistosome cercariae do not live longer than 48 hours in water can also be used in prophylaxis in certain circumstances.

Researches on cercaricidal substances have mostly centred about the effects of chlorine. WITENBERG and YOFE [this *Bulletin*, 1938, v. 35, 600] found chloramine more efficient than gaseous chlorine or sodium hypochlorite, the concentrations necessary being 0·22 part per million residual after 10 minutes' application for chloramine, 0·42 for sodium hypochlorite and 0·6 for gaseous chlorine. MAGATH's experiments [this *Bulletin*, 1943, v. 40, 156] indicated that chlorination of 0·2 part per million [residual of 0·1 p.p.m. after 30 minutes] kills cercariae of *S. mansoni* in 30 minutes. OLIVER GONZÁLEZ, BIAGGI and RIVERA LEÓN [this *Bulletin*, 1946, v. 43, 347] suggest from experimental results that a minimum exposure of 20 minutes to the effects of a chlorine solution yielding a minimum chlorine residual of 0·5 part per million, may be sufficient to render cercariae non-infective. KRAKOWER [this *Bulletin*, 1941, v. 38, 376]

subjected the cercariae of *S. mansoni* to a variety of physical conditions and found that their normal span of life in rain water is 24–48 hours, rarely 72 hours. They survive up to 14 days at 5°–6°C. but remain motionless, while freezing is rapidly fatal. Above 34°C. the mortality increases, and at 45°C. all die in 30 minutes. Strong electric light induces activity and shortens the span of life, while ultraviolet light and direct sunlight are both fatal, but the heat of the sun may also be an adverse factor in this instance. Extremes of *p*H outside the 4·6–10 range are fatal, and cercariae are rapidly killed in a 1·5 per cent. solution of sodium chloride.

Treatment.

The efficacy of prevention in an anti-bilharzial scheme must necessarily be greatly enhanced by concurrent treatment of the infected population, which stems the source of snail-infection at its origin ; but the prolonged and tedious procedure of present-day methods of chemotherapy in schistosomiasis is very unsuitable for mass treatment. In this connexion the researches of ALVES [this *Bulletin*, 1945, v. 42, 815] and ALVES and BLAIR [*ibid.*, 1946, v. 43, 344] on an intensive treatment with sodium antimonyl tartrate in Southern Rhodesia are most opportune, and have an important bearing on the present problem. These authors devised a course of treatment of only 2 days' duration, which consists of six intravenous injections each of 1–2 grains of S.A.T. In a trial of 100 cases, all positive by intradermal tests and by examination of stools or of urine, none was passing eggs two months after treatment, and a high proportion were negative by the skin test. Toxic complications were unimportant and transient. This treatment was subsequently modified to a course of one day only, with smaller dosage [ALVES, below, p. 752], which was tried out on a group of 131 cases, all positive by the skin test. Four weeks later none of these was passing eggs. While the " follow-up " of these cases is as yet incomplete, and the possibility of relapses is admitted, the importance of the treatment is manifest, for it provides a means of rapidly disinfecting an infected population for a time at least, which would offer " a breathing-space in the struggle to break the life-cycle in bilharziasis, since our snail-killing will be at a peak at, and immediately after, the time when the population's infectivity is at its lowest, and those adult snails which escape killing will also escape infection."

If the promise held out by these researches is fulfilled, a great advance in the control of schistosomiasis will have been achieved.

SUMMARY OF RECENT ABSTRACTS.*

VII. HELMINTHIASIS.

General.

VASILKOVA (p. 569) has examined the water of the river Moskva, in Russia, for helminth eggs. The main source of contamination was the effluent from a sewage works, and in water from this source 4,500 eggs per cubic metre were found, including those of *Ascaris*, *Trichuris*, *Taenia* and *Diphyllobothrium* ; *Enterobius* and *Dicrocoelium* eggs were found in the river water. Some of the eggs were viable. A degree of natural cleansing of the river water takes place by settlement, but better methods of purifying sewage water are needed. In the meantime, people may infect themselves from the river.

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* The information from which this series of summaries has been compiled is given in the abstracts which have appeared in the *Tropical Diseases Bulletin*, 1945, v. 42. References to the abstracts are given under the names of the authors quoted and the pages on which the abstracts are printed.

NIÑO (p. 473) discusses appendicitis in which there is associated helminth infestation of the appendix. He found worms in 3·17 per cent. of 1,763 appendices examined; in by far the majority of cases the worm was *Enterobius vermicularis*.

OLIVER-GONZÁLEZ and TORREGROSA (p. 45) have isolated a substance from certain helminths infesting man, which is related to human isoagglutinins.

A Symposium on Anthelmintics (p. 570) has been published in the United States.

ROGERS (p. 299) has made a very thorough study of the anthelmintic activity of hexylresorcinol and tetrachlorethylene, using the perfused small intestine of rats infested with *Nippostrongylus muris* for the purpose. Details of the many observations should be sought in the original abstract, but the main conclusions are that the efficiency of hexylresorcinol is reduced by sodium taurocholate, and that the drug is adsorbed on to mucin, which prevents its penetration into the parasites. The latter appear to stimulate the formation of mucus in the intestine, and are, to a very considerable extent, protected by the mucus on the intestinal wall. Tetrachlorethylene, on the other hand, stimulates *N. muris* to leave mucus and to enter fluids in the intestinal lumen; it is not inhibited by bile salts, and acts rapidly in the rat. Sodium laurate and sodium oleate show intrinsic anthelmintic properties; the former activates hexylresorcinol more than the latter.

PARANJAPE *et al.* (p. 571) have investigated the anthelmintic action of certain synthetic lactones and compounds allied to santonin. In their work they used earthworms; commenting on this fact, LAPAGE gives reasons why *Ascaris* of the pig would provide a more satisfactory test.

Trematodes.

General.—SILVEIRA (p. 46), in a discussion of pulmonary schistosomiasis, notes that this condition is much less common in *S. mansoni* than in *S. haematobium* infections, and explains this by reference to routes available, in the venous system, to each of these trematodes. Nevertheless, pulmonary schistosomiasis due to *S. mansoni* is not uncommon. There are two stages: acute (during the stage of migration through the lung) which is the toxaemic form and may even be fatal; and chronic (due to adult worms or eggs in the lung). Clinically there are two forms, with respiratory symptoms or with symptoms of embarrassment of the pulmonary circulation. The only certain diagnosis is the finding of eggs in the sputum, since radiological signs are not characteristic.

Schistosoma haematobium.—Vesical schistosomiasis is prevalent in Angola. In one area SARMENTO (p. 1015) found infection in 60 per cent. of children, and in 21·5 per cent. of adults. ANDREASEN and SURI (p. 742) report what appears to be the first recorded case of infection with *Schistosoma haematobium* contracted in India. [The importance of such a finding is sufficiently obvious; the disease was well established in this patient, and the authors think that he probably acquired it in his home village.]

GORSSE and ACCART (p. 395) review the results of treatment of over 200 cases of urinary schistosomiasis. They argue that the best estimate of treatment can be obtained by cystoscopy, and they describe the appearances to be seen by this means at different stages of the infection. The results of treatment with tartar emetic, Fouadin and anthiomaline were not satisfactory, the last of these being the best. Nevertheless, antimony, though not specific, is the most useful drug, but in some cases seems to be insufficient by itself. An intensive course of treatment of schistosomiasis with a preparation of sodium antimonyl tartrate is described by ALVES (p. 815). The whole course

consists of a total dosage of 12 mgm. of the drug per kgm. body weight, and the injections are given intravenously at intervals of 2 to 2½ hours over a period of 30 hours, with a break of some 16 hours after the first day of treatment. The injections are given very slowly, and the drug is well diluted in glucose-saline. Results appear to be promising.

STEPHENSON (p. 572) has treated nine patients, infested with *Schistosoma haematobium*, with stilbamidine, but concludes that the action of this drug is too uncertain to justify its routine use in urinary schistosomiasis.

S. mansoni.—In Pernambuco, infection with *S. mansoni* is common, and MAGALHÃES (A.) *et al.* (p. 1016) show that the infection rate is highest in late childhood and young adult life. Males are rather more commonly affected than females.

DI GIACOMO and MAYER (p. 47) make the point that infection with *S. mansoni* may be very insidious, and that stool examination should be made on all persons from endemic areas, whether or not there are suggestive symptoms.

WRIGHT and ROBERTS (p. 215) describe the early symptoms of infection with *S. mansoni* in a boy who, shortly after contracting this infection, showed creeping eruption which the authors think was due to larvae of *S. mansoni*. At the time when the creeping eruption was noticed, the boy was suffering from urticaria ; he subsequently developed intense eosinophilia.

BERCOVITZ *et al.* (pp. 47, 572) found small ulcers on proctoscopic examination of recruits, in Porto Rico, who had eggs of *S. mansoni* in their faeces. The blood picture showed little departure from the normal.

ALMY and HARPER (p. 646) report a case of chronic infection with *S. mansoni*, in which Banti's syndrome developed. ALMY and HARPER (p. 815) also describe a case of long-standing infection with *S. mansoni*, in which there were associated signs of Banti's disease.

SANABRIA (p. 396) describes two patients, with bilharzial myocarditis, in whom the Stokes-Adams syndrome was present. MEIRA and RAMOS (p. 572) discuss two forms of myocarditis which may occur in infestation with *S. mansoni*, but in part of a thesis on *S. mansoni* infection, MAGALHÃES (B. F.) and DIAS (p. 1016) make a note of the fact that in 22 autopsies they failed to find myocardial lesions, and that ova have not been found in the heart muscle. They think, therefore, that it is highly improbable that there is a cardiac form of the disease.

CRAM *et al.* (p. 646) have shown that the snail *Tropicorbis havanensis*, indigenous to the United States, is susceptible to infection with *S. mansoni*.

Bulinus truncatus is a carrier of bilharzia in the Fayoum Province of Egypt. BARLOW and ABDEL AZIM (p. 1017) describe control measures used in Egypt against this and other snails. There are two main methods : mechanical clearance of small streams by means of standardized hand nets, and the use of copper sulphate in larger canals. For the latter, concentrations of 15–50 parts per million are required in field work. Snails live a long time, but probably not more than 2 years ; desiccation for 40 days cannot be relied upon to kill them, since they have been known to revive after 12 months' desiccation in mud. JANSEN (p. 1018) has found that slaked lime in a strength of 4–5 parts per 1,000, and copper sulphate in a strength of 2 parts per 1,000, are effective in killing *Australorbis centrimetralis*, the host of *S. mansoni* in Pernambuco.

KRAKOWER *et al.* (p. 133) have found that eggs of *S. mansoni* in guineapigs kept on a diet deficient in vitamin C, tend to show disintegration of the shells ; deficiency of vitamin C did not, however, interfere with the development of *Schistosoma*.

S. japonicum.—An account of the symptoms of the early stage of schistosomiasis japonica is given by THOMAS and GAGE (p. 1018). There is usually fever, with headache, cough, possibly abdominal symptoms and, in some cases, urticaria. The liver is usually enlarged and tender, the spleen less commonly so. Eosinophilia is characteristic. Eggs are found in the faeces some 6–10 weeks after infection; they may be present in patients who have had no more than trivial symptoms.

In the *Bulletin of the U.S. Army Medical Department* (p. 1019) the treatment of schistosomiasis japonica is discussed, and Fouadin and tartar emetic are the drugs advocated. Each may be toxic, and each should be injected slowly; Fouadin should be tried first. For details of administration the original abstract should be consulted.

Other trematodes.—STEPHENSON (p. 474) has found that *Fasciola hepatica* will live for 60 hours at 36°C. in a solution containing NaCl, KCl, $CaCl_2$, borax and glucose, of *p*H 8·6. This is adequate for the preliminary testing of anthelmintics; in such tests carbon tetrachloride was found to be innocuous, though it is probably the best anthelmintic in man.

WITENBERG (p. 396) has found a fluke, *Clinostoma complanatum*, in man; it caused laryngo-pharyngitis. This infection is apparently due to the eating of fish infested with metacercariae of the fluke.

CORT (p. 905) discusses the germ-cell cycle in the digenetic trematodes. The subject is complex, and cannot briefly be dealt with; the original should be consulted by those interested.

Cestodes.

In a series of four papers, TÖTTERMAN (p. 215) discusses the anaemias which occur in a small proportion of people infested with *Diphyllobothrium latum*. He estimates that about 14 per cent. of people in Finland are infested by this worm. The well-known anaemia is indistinguishable from pernicious anaemia, but there is another and more common form, a light hyperchromic anaemia, which he regards, not as a stage in the development of the former, but as a separate condition. In this anaemia liver preparations have no effect, but improvement follows administration of a vermifuge, whereas in the "pernicious" form liver is useful. The light anaemia is probably due to absorption of toxins from the worm, which, alone, will not cause the "pernicious" form.

Treatment of the "pernicious" anaemia with yeast, which is rich in Castle's extrinsic factor, has given good results, but the author has not been successful with certain extracts of hog stomach. He argues that the "pernicious" anaemia of *D. latum* infestation occurs in patients who have become sensitized to the tapeworm, and quotes his own experiments, which showed that in sensitized persons, but not in normal controls, administration by injection of an alcoholic extract of the worm tended to produce a "pernicious" form of anaemia.

GIBSON (p. 396) reports the discovery of species of *Diphyllobothrium* in trout in England, and UNSWORTH (p. 397) discusses the recent findings of tapeworms of this genus in fish and in birds in England and Ireland. He concludes that the evidence is against their being *D. latum*, but, in comment, LAPAGE suggests that the relationship between the tapeworms of birds and *D. latum* needs further study. BAYLIS (p. 906) also discusses the species of *Diphyllobothrium* found in trout and in birds in the British Isles, and differentiates them from *D. latum*.

DIXON and HARGREAVES (p. 907) report on 284 cases of cerebral cysticercosis. In 89 per cent. of proved cases radiographic examination of the skull failed to show the parasites, and the point is made that only in a minority of cases do the degenerative changes in these intracerebral cysts go on to calcification.

The authors discuss prognosis, and, in comment, MacArthur points out that relapse may follow a symptom-free period lasting as long as 20 years. The original paper should be read by those interested in this condition.

Arana and Asenjo (p. 908) have made ventriculographic examinations in 20 cases of cerebral cysticercosis in which the parasites were sub-tentorial. All cases were verified. The radiological findings should be studied in the original.

Selman (p. 816) describes a case of eosinophilia of the blood and of the cerebrospinal fluid, in a patient who showed signs of meningeal irritation. The author thinks that this was probably a case of cerebral cysticercosis. A similar case is referred to by Applebaum and Wexberg (p. 816).

Mazzotti (p. 647) gives information on cysticercosis in Mexico, and again refers to the high proportion of positive results obtained, in infestations with *T. saginata*, by examination of the perianal region by means of swabs. This suggests the possibility of auto-infection, and similar findings have been made in the case of *T. solium*, but not, apparently, to anything like the same extent, probably because the proglottides of *T. solium* do not emerge spontaneously, as do those of *T. saginata*, but only with the faeces.

The same author (pp. 134, 398) made 108 examinations of the perianal region, by means of the Graham adhesive cellulose tape method, in 10 persons infested with *Taenia saginata*. Of these examinations, 85 per cent. were positive, whereas with direct smear examination of faeces, the proportion was very much smaller. Eggs were also found on other areas of skin between the neck and the knees, and on the underclothes. On examining the proglottides of the worm he found that the branches of the uterus communicate with the exterior when the proglottid is detached, and that disintegration is therefore not essential for expulsion of eggs.

Niño (p. 909) thinks that Acranil, an acridine derivative of the mepacrine type, is the ideal anthelmintic for the treatment of infestation with *Taenia saginata*. Of 41 patients, 34 were cured by a single treatment, and four others after more than one. Details of administration are given in the original abstract.

Rivas *et al.* (p. 910) give details of the statistics of hydatid disease in patients treated at the Institute of Clinical Surgery, Buenos Aires. The amount of information given cannot satisfactorily be summarized, and the original abstract should therefore be consulted.

Barrett and Thomas (p. 474) have written a long paper on pulmonary hydatid disease. It is not possible to do justice to all the points raised, for which the original should be consulted, but certain statements may be noted. The presenting symptom is usually haemoptysis, but the first signs and symptoms may be due to anaphylaxis. Sudden expectoration of a large amount of clear, salt-tasting fluid is diagnostic of the rupture of a simple cyst. Pulmonary hydatid cysts should never be aspirated. The parasite should be removed at the earliest possible moment ; the safest way to enucleate a simple cyst is to treat it as a lung abscess, but in a selected group of cases the treatment of choice is lobectomy.

Castro (p. 573) discusses hydatid disease of bone. Prognosis in these cases is grave, and for affected bones of the limbs, amputation is usually necessary. Hydatid disease of the spine is always fatal. Howorth (p. 817) also refers to the fact that treatment of hydatid cysts of bone is still unsatisfactory.

Treatment of infestations with *Hymenolepis* in children, by means of male fern given in "cycles", was found unsatisfactory by Podyapolskaya and Isaicheva (p. 573), who therefore experimented with other drugs given in association with male fern. Of these the most effective was methylene blue,

but yatren was also useful. For details of administration the original abstract should be consulted. GORIACHEVA (p. 575) has tried this method, and regards it as the best yet available; he prefers it to the use of pumpkin seeds or of full doses of male fern, both of which he tested.

In a study of the vitamin requirements of cestodes, ADDIS and CHANDLER (p. 302) found that *Hymenolepis diminuta* was markedly affected by lack of vitamins in the diet of the host, if the latter was a female rat, but not if it was a male (Chandler). They therefore worked with female rats, and discovered that the vitamin concerned was riboflavin. If this was withheld, the number and size of the infesting cestodes were smaller than in rats on full diet, and the longer the vitamin had been withheld, the more marked the effect. On the other hand, when vitamins A, D, E, and B, were lacking, the worms grew rather longer than shorter. The cestodes obtain their protein by absorption direct from the mucosa of the host, not from the contents of the intestine [and presumably they obtain riboflavin in the same way].

KOURÍ (p. 477) reports that up to 1944 more than 70 cases of infestation with *Inermicapsifer cubensis* had been reported, usually in young children. Man is probably not the normal host, and appears to be an unfavourable host, but examination of a large number of mammals, acari, insects and crustacea has failed to reveal the parasite.

Charles Wilcocks.

[*To be continued.*]

MALARIA.

PROKOPENKO, L. I. [**Analysis of the Causes of the Severe Epidemic of Malaria in 1942 in Urgut District of the Samarkand Province and Measures for the Prevention of Increase of Malaria Morbidity in 1943.**] *Med. Parasit. & Parasitic Dis.* Moscow. 1945, v. 14, No. 3, 15–33, 5 figs. [In Russian.]

The author records the results of observations made by an expedition, organized by the Moscow and Uzbek Malaria Institutes, for the study of the causes of a serious outbreak of malaria in the province of Samarkand (Middle Asia) and to devise measures for its control. A detailed analysis is given of the epidemiological situation in the Urgut district, which represented the focus of the epidemic. This area is characterized by a high endemicity of malaria of all the three types, the malignant tertian form being predominant. There are two efficient vectors, *A. maculipennis sacharovi* and *A. superpictus*, and abundant breeding places, in the form of rice-fields, swamps and a network of canals. By the time the expeditions arrived and were in a position to undertake the necessary anti-malarial measures, fully 100 per cent. of the local population (about 40,000) had had malaria, and a high proportion among them were carriers. With the view to dealing with the existing situation and to preventing an epidemic in 1943 the following measures were adopted :—

(1) Systematic anti-relapse treatment with acriquine (=mepacrine) (0·3 gm. daily in single dose), to which in the last cycle plasmocide (=pamaquin) was added; (2) chemoprophylaxis of the entire population with acriquine+plasmocide (0·3 gm. acriquine+0·04 plasmocide on two successive days followed by an interval of 5 days); (3) early detection of all acute cases of malaria and parasite-carriers, and their systematic drug treatment; (4) monthly examination of the population for the detection of carriers and for observation of the indices.

These measures against the parasite in the human host were combined with anti-mosquito measures, including improvements affecting mosquito breeding places.

In undertaking all these measures the investigators realized that methods which were capable of eliminating malaria from localities with a low incidence of malaria were insufficient to cope with the infection in a highly affected focus. Nevertheless, the expeditions have succeeded in their main task—to prevent a fresh epidemic outbreak. The anti-malarial campaign resulted in a lowering of the incidence of malaria, in an absence of severe forms (coma, etc.) without fatal cases, as well as in raising the labour output of the population.

C. A. Hoare.

YAGUJINSKAYA, L. V. [**Malaria Vectors in the Northern Part of the Urgut District, after the Observations of 1943.**] *Med. Parasit. & Parasitic Dis.* Moscow. 1945, v. 14, No. 3, 47–56, 6 figs. [In Russian.]

This paper is devoted to the results of a study of the anopheline population in the Urgut District of the Samarkand Province (Middle Asia), in which a severe outbreak of malaria occurred in 1942 [see PROKOPENKO, above]. A detailed description is given of the bionomics of the mosquitoes, of which the most common are *A. bifurcatus*, *A. maculipennis sacharovi* and *A. superpictus*, while *A. algeriensis* and *A. pulcherrimus* occurred only singly. *A. hyrcanus* has never been found in dwellings. In view of the predominance of *A. maculipennis sacharovi*, as compared with the other species, during the epidemic season, and on account of its known epidemiological peculiarities, this mosquito is regarded as the most important local vector of malaria. This conclusion is fully supported by the oöcyst and sporozoite rates revealed by dissection.

C. A. Hoare.

FLOCH, H. & ABONNENC, E. Sur *A. darlingi* Root 1926, en Guyane française. Gîtes larvaires, morphologie et moeurs. [*A. darlingi* **in French Guiana : Breeding Places, Morphology and Habits.**] *Publ. Inst. Pasteur Guyane.* Cayenne. 1943, No. 65, 7 pp. [11 refs.] Sur le rôle de *A. darlingi* Root 1926 dans la transmission du paludisme en Guyane française. [**The Rôle of** *A. darlingi* **in Malaria Transmission in French Guiana.**] *Ibid.* No. 71, 10 pp. [Summary taken from *Rev. Applied Entom.* Ser. B. 1946, Apr., v. 34, Pt. 4, 57–8.]

In the first paper, data on the breeding places of *Anopheles darlingi*, Root, and the house-frequenting habits of the adults are reviewed from the literature and from observations in French Guiana, where it was first recorded in 1934. Adults and larvae have since been found along the whole length of the island of Cayenne and at various places in the interior but not in the town of Cayenne, which is swept by Atlantic winds. The breeding places differ greatly but are usually in open situations sheltered from wind and sometimes partly shaded from the sun. The water is acid in reaction and of low mineral content and the vegetation varied. A study of eggs laid by females from different localities in French Guiana showed that there were forms corresponding to those described by Root and by Galvão, Lane and Corrêa and an intermediate form. Sometimes they occurred alone and sometimes all three together in one batch. The adults reared from these eggs showed no differences of any consequence, and the authors conclude that *A. darlingi* cannot at present be divided into varieties. *A. darlingi* represented 91 per cent. of the *Anopheles* taken in houses throughout the year but only 12 per cent. of those taken in woods.

In the second paper, it is pointed out that it is most abundant in June–August when malarial endemicity is increasing and that it prefers to feed on man although it has been observed to attack fowls and ducks and is occasionally taken in traps containing horses. Data are given from the literature on its natural infection with malaria parasites in other countries. Dissection of 542 females taken in French Guiana showed seven to be infected, six with oöcysts and two with sporozoites. As the mosquitos were not from large centres of population, *A. darlingi* is thought to be an important local vector in spite of this comparatively low infection rate. Of females that survived for more than four days after being fed on gametocyte carriers, five out of 14 became infected with *Plasmodium falciparum*, the commonest malaria parasite in French Guiana, and one out of six with *P. vivax*. In one instance infection with *P. falciparum* developed to the sporozoite stage.

Floch, H. & Abonnenc, E. Sur *A. aquasalis* Curry, 1932. *Publ. Inst. Pasteur Guyane.* Cayenne. 1943, No. 68, 9 pp., 2 figs. *A. aquasalis* Curry 1932 et paludisme en Guyane française. Infection naturelle et infection expérimentale. [**Experimental and Natural Infection of** *A. aquasalis* **in French Guiana.**] *Ibid.* No. 72, 8 pp. [Summary taken from *Rev. Applied Entom.* Ser. B. 1946, Apr., v. 34, Pt. 4, 58–9.]

The species of *Anopheles* of the subseries *oswaldoi* known to occur in French Guiana when these papers were written were *A. ininii*, Senevet & Abonnenc, and *A. oswaldoi*, Peryassú, both of which had been found only in the interior, and *A. aquasalis*, Curry (previously referred to as *A. tarsimaculatus*, Goeldi). In view of the discovery in Venezuela of the three closely related coastal species, *A. nuñez-tovari*, Gabaldon, *A. rangeli*, Gabaldon, Cova-García & López, and *A. goeldii*, Rozeboom & Gabaldon, data on the wing and tarsal colouring of these three and *A. oswaldoi* and *A. aquasalis* are quoted from Gabaldon & Aguilera. However, they do not make accurate differentiation possible and in order to identify with certainty the mosquitos occurring on the coast of French Guiana and referable from examination of females to *A. aquasalis*, progeny were reared from several caught in nature. Examination of the adults and male hypopygia showed them to agree with *A. aquasalis*. There was considerable variation among eggs of a single batch. This is the only species of *Anopheles* occurring in houses in Cayenne, but over the rest of the coast it represents 51 per cent. of the *Anopheles* taken in woods but only 6 per cent. of those taken in houses. It attacks both man and animals. Larvae were found at all seasons and occurred in fresh and brackish water. They were very adaptable, surviving transfer from salt water (19 gm. sodium chloride per litre) to fresh and from fresh to salt.

Further information is given in the second paper on the occurrence of *A. aquasalis* in Cayenne, where it is found on outside walls and in dark corners of kitchens, ground-floor rooms and sheds and rarely in mosquito nets. Dissection of 117 females from various parts of the colony failed to reveal any natural infection with malaria parasites. However, undoubted cases of locally acquired malaria occurred in 1940 in Cayenne where there is no other Anopheline, and experimental infection was obtained with *Plasmodium falciparum* in seven out of 30 females that survived for more than four days and with *P. vivax* in ten out of 28. In one case, infection with *P. falciparum* developed to the sporozoite stage. *A. aquasalis* thus appears to be more susceptible to *P. vivax* than *A. darlingi*, Root [*cf.* preceding abstract], but it is thought to be only a secondary vector of malaria in view of its habit of feeding indifferently on man or animals.

FLOCH, H. & DE LAJUDIE, P. Sur les divers indices endémiques du paludisme en Guyane française. [**Endemic Indices of Malaria in French Guiana.**] *Publ. Inst. Pasteur Guyane.* Cayenne. 1945, No. 107, 10 pp. [11 refs.] [Summary taken from *Rev. Applied Entom.* Ser. B. 1946, Apr., v. 34, Pt. 4, 60.]

The results of recent malaria surveys made in the interior of French Guiana are given and compared with similar data for Cayenne. The spleen, parasite, and gametocyte rates were 44, 24 and 7 in the interior and 12, 6 and 0·3 in Cayenne. *Plasmodium falciparum* was responsible for 85 per cent. of cases, whereas 68 per cent. were attributable to *P. vivax* in 1917. A list is given of the 21 species of Anophelines known to occur in French Guiana. All have been recorded in earlier papers of this series except an unidentified species of the subgenus *Stethomyia* of *Anopheles*. *A. darlingi*, Root, is stated to be the principal vector of malaria, though it has not yet been taken in the regions dealt with in this survey. *A. aquasalis*, Curry, and *A. triannulatus*, Neiva & Pinto (*bachmanni*, Petrocchi) have been experimentally infected but attempts to infect *A. pessôai*, Galvão & Lane, and *A. mediopunctatus*, Theo., failed.

MUSPRATT, J. **On** *Coelomomyces* **Fungi causing High Mortality of** *Anopheles gambiae* **Larvae in Rhodesia.** *Ann. Trop. Med. & Parasit.* 1946, Apr., v. 40, No. 1, 10–17, 2 figs. on 1 pl.

The finding of fungal parasites of the genus *Coelomomyces* in larvae of *Anopheles gambiae* at Livingstone, Northern Rhodesia, in March 1941, led the author to make further observations, until May 1945.

He was able to distinguish four types of the parasite. Type *a* was the commonest and was also the most important, for in nature it killed large numbers of larvae of *A. gambiae*. It was seen occasionally in larvae of *A. squamosus* and *A. rufipes* and once in *A. rivulorum*, but it seems unlikely that the fungus seriously affects larvae of the *funestus* series. Larvae of *A. pretoriensis* became infected when transferred to an infected pool. Larvae of *A. coustani* and *A. rhodesiensis*, taken from water containing infected larvae of *A. gambiae*, showed no sign of fungus, and no culicine larvae (except a few *Culex simpsoni*) were infected. Laboratory-bred larvae have not yet been successfully infected.

Type *b* is rarer than type *a*, and has been observed in larvae of *A. gambiae* and *A. squamosus*. Type *c* was found only in larvae of *Aëdes scatophagoides*, and type *d* in the stem of a sedge (*Cyperus* sp.) but not in any mosquito larva or any other aquatic insect.

The fungus seems to be associated with the heavy, dark-brown, loamy clay locally known as " mopane " clay. Most of the infected pools are exposed to sunlight ; infected larvae are found only during three or four months in the wet season, that is, from December onwards, and the mortality of *A. gambiae* larvae in observed pools in that period is estimated to be often as high as 95 per cent.

The author describes the appearance of the infection in the larvae, and the process of germination. He is convinced that the matter is worthy of a more thorough investigation, particularly as regards the possibility of using the fungus in the biological control of *Anopheles gambiae*. *H. S. Leeson.*

RABONI, C. Alcuni sintomi respiratori nell'infezione malarica primitiva. [**Respiratory Symptoms in Primary Malaria.**] *Riv. Patol. e Clin. d. Tubercolosi.* 1944, May–June, v. 18, Nos. 5/6, 96–104. [11 refs.]

STONHAM, F. V. **Traumatic Rupture of Large Spleens.** *Indian Med. Gaz.* 1945, Nov., v. 80, No. 11, 547–11, 3 figs. (1 on pl.).

Malaria is by far the commonest cause of enlargement of the spleen in Asiatics in India. Rupture may be spontaneous, or caused by trivial violence, though more usually it is due to traffic accidents, or brawls, and is associated with other injuries. In the majority of cases shock and haemorrhage are so severe that the patient quickly succumbs, so that probably only one in every 20 of such patients reaches hospital alive, but spontaneous arrest of haemorrhage by clotting sometimes occurs, even after severe damage. Delayed haemorrhage from the injured spleen is usually due to such a clot giving way. The malarial spleen, unlike that in acholuric jaundice or splenic anaemia, is seldom adherent to surrounding tissues. Kala azar produces large, soft, fragile spleens, which later become firm and fibrous ; these may be ruptured by violence or by tearing of the capsule when spleen puncture is done. Enteric fever, tumours and blood disorders are not important aetiological factors in traumatic rupture of the spleen in Asiatics.

The patient with ruptured spleen is profoundly shocked, with local signs of trauma, and possibly haematuria from coincident damage to the left kidney. The abdomen becomes distended, but true rigidity is usually absent. The pulse is rapid and of poor volume, and the blood pressure is low. X-ray examination, which should not be done if the diagnosis can be made without it, may show raising of the left cupola of the diaphragm. Fixed dullness in the left flank, with shifting dullness in the right flank (Ballance's sign) is unreliable, as it depends on the size of the spleen and the amount and site of the blood clot. Liver dullness may be diminished. There is usually little or no recovery from the initial shock and the condition deteriorates progressively unless operation is undertaken promptly. A high operative mortality must be accepted if lives are to be saved, and delay is justified only when the patient's condition is so low that immediate operation would be fatal, or in cases where the injury occurred more than 12 hours previously and the patient's condition is stationary. The author does not think that time should be spent in resuscitation and transfusion, as these may cause further bleeding and add to the shock.

Cyclopropane is the anaesthetic of choice, though chloroform with free administration of oxygen was used in the majority of the author's cases in Persia, Iraq and India. Continuous pentothal administration was used in some of his later cases. A continuous intravenous infusion of saline, or of blood if available, is started at the commencement of the operation. A long mid-line incision is recommended, to which a transverse incision may be added if more room is required. As blood tends to remain fluid when shed into the peritoneal cavity, the peritoneum is opened by a small incision and as much as possible of the fluid blood is sucked out by a Higginson's syringe, to be added to the transfusion fluid after straining. The peritoneum is then opened widely, the clots are removed, and the operation completed in the usual manner. A sudden worsening of the patient's condition often occurs as the spleen is dislocated. Drainage is not employed unless there has been injury to the tail of the pancreas. Post-operative transfusion is continued till the systolic blood pressure is 100 mm., but failure to recover from shock is often seen. Simultaneous rupture of the left kidney can, in most cases, be treated on conservative lines. A left pleural effusion of moderate amount is of no significance, but associated injury to the chest is likely to cause trouble.

W. L. Harnett.

KYKER, G. C., CORNATZER, W. E. & MCEWEN, Mildred M. **The Ultraviolet Irradiation of Quinine.** *J. Biol. Chem.* 1946, Feb., v. 162, No. 2, 353–61, 2 figs. [16 refs.]

It is known that solutions of the cinchona alkaloids exposed to light of short wave-length undergo some change whose nature has not been definitely established. In the present investigation the photodecomposition of quinine and quinidine has been studied following irradiation with sunlight or an ultraviolet lamp. The antimalarial activity of the irradiation products will be reported on at a later date. Solutions of pure material containing 5 mgm. quinine per ml. were exposed to sunlight in very dilute sodium hydroxide (mixed with alcohol to retain the base in solution), in water and in different strengths of hydrochloric acid in Pyrex as well as in soft glass containers. Control samples were kept in the dark. Estimations of the amount of quinine still present were made at intervals up to 275 days in each series by three different methods. In the first two methods the turbidimetric procedure of KYKER, WEBB & ANDREWS (*J. Biol. Chem.*, 1941, v. 139, 551) was employed, with and without previous ether extraction of base, respectively. By the third method, specific optical rotation was determined. In the irradiation experiments with ultraviolet light, quartz cells which freely transmitted the wave-lengths of light absorbed by the alkaloid, served as containers. Solutions of quinine dihydrochloride and sulphate and quinidine sulphate were used for exposure. Turbidimetric and fluorimetric methods of analysis were employed. The results of irradiation with u.v. light were qualitatively similar to those obtained by exposure to sunlight, but the former method was more effective in causing photodecomposition and there was only slight discoloration of the solutions. The results of analysis by the different methods did not give very concordant results. It appeared, however, that the amount of decomposition depended on the *p*H of the solution, on the concentration of alkaloid present and on the optical properties of the containers, but not on the nature of the alkaloidal salt. Control tubes kept in the dark showed no discoloration or alteration in quinine content. No evidence of the chemical nature of the changes occurring was obtained. *J. D. Fulton.*

BISHAY, A. **Quinine Amblyopia.** *Brit. J. Ophthalm.* 1946, May, v. 30, No. 5, 281–7, 4 perimeter charts.

SHIERS, D. **Cerebral Excitement following Mepacrine Therapy.** [Memoranda.] *Brit. Med. J.* 1946, May 18, 762–3.

On three separate occasions in 1945 a soldier felt and showed signs of great mental exhilaration and other emotional disturbance after taking mepacrine. There was no personal or family history of mental instability and the Wassermann reaction of his blood was negative. The symptoms are well described in the present report, which relates to the third occasion, after his admission to the Royal Masonic Hospital in December 1945 for an attack of benign tertian malaria.

He was given mepacrine, 0·7 gm. daily for 2 days, then 0·6 gm. daily for 7 days. "Almost immediately he was seized with a feeling of extreme exhilaration and well-being. He began almost to burst with energy, running instead of walking, and doing everything at top speed. His mind became choked with ideas, which occurred at all times of the day and night. While many of these never reached maturity some of them resulted in the patient writing poems and creating new designs for houses and buildings. At times, too, he was seized with an uncontrollable desire to cry and as a result would weep copiously although inside he felt, so he said, extremely happy."

The first occasion was in February 1945 in Assam, when he took suppressive doses of mepacrine, 0·1 gm. daily, with similar effects; the second was in August 1945 when he had his first true attack of malaria and took mepacrine 0·2 gm. t.d.s. for 5 days in addition to quinine, and, later, pamaquin; again the same effects were produced during the taking of mepacrine.

He slowly recovered from this third attack on ceasing to take mepacrine and receiving phenobarbitone. [For other references to mental effects due to mepacrine (atebrin) see this *Bulletin*, 1937, v. 34, 151, 159; 1938, v. 35, 516; 1939, v. 36, 872; 1941, v. 38, 337; 1945, v. 42, 9, 253, 629, 784. The author refers also to ALLEN, *J. Med. Ass. Georgia*, 1937, v. 26, 62.]

J. F. Corson.

KING, E. J., GILCHRIST, M. & TARNOKY, A. L. **Excretion Products of Mepacrine: a Spectrophotometric Study.** *Biochem. J.* 1946, v. 40, No. 1, Proc. Biochem. Soc. iii.

SPINKS, A., TOTTEY, Mary M. & MAEGRAITH, B. G. **The Pharmacology of Paludrine and some other New Antimalarials.** *Biochem. J.* 1946, v. 40, No. 1, Proc. Biochem. Soc. i.

SPINKS, A. & TOTTEY, Mary M. **Studies on Synthetic Antimalarial Drugs. XV. Hydrolytic Determination of Paludrine.** *Ann. Trop. Med. & Parasit.* 1946, Apr., v. 40, No. 1, 101–12, 7 diagrams.

The method employed by the authors for the estimation of Paludrine [this *Bulletin*, 1946, v. 43, 400], now in use for one year, has been slightly modified, and the time required for hydrolysis has been greatly reduced. Special precautions such as the need for clean apparatus and purity of reagents, as well as points in technique, are fully described. Briefly, the method consists in basifying the material containing the drug with NaOH, followed by extraction with a benzene-ethanol mixture. The base is taken up in N/4 hydrochloric acid and hydrolysed to *p*-chloroaniline at 20–25 lb. pressure for 3–4 hours. The latter substance is then diazotized and coupled to form an azo dye and matched against a standard in a photoelectric or visual colorimeter within an hour of preparation. The procedures used with different materials such as plasma, blood, urine, faeces, bile or tissues, vary slightly in detail; for these the original should be consulted. With plasma and blood the method can be used for concentrations down to 50 μgm. per litre. With lower concentrations a modified coupling method is employed in conjunction with a Spekker absorptiometer, and the sensitivity is increased 3–5 times.

A special investigation was made regarding the best conditions of hydrolysis for Paludrine and closely related compounds to *p*-chloroaniline; these are embodied in the above method. It was found that Paludrine can be sufficiently hydrolysed even at 100°C. to allow of estimation, if an autoclave is not available. N-β-sulphatoethyl-*m*-toluidine was found to be a more satisfactory coupling agent than β-1-naphthylethylenediamine. Using the former reagent, the authors investigated the stability of the dye solution. The value for the extinction coefficient at the wave-length of maximal absorption was unaltered after 17 hours, but there was at that time an increased absorption at lower wave-lengths. Hence the recommendation to examine the dye solutions within one hour after development of colour, if a spectrophotometer is not available. Isolation of Paludrine from the urine of human subjects receiving the drug showed that the amount recovered was in fair agreement with that obtained by the hydrolytic method of estimation, and indicates that it is a suitable procedure.

J. D. Fulton.

J. Amer. Med. Ass. 1946, Apr. 20, v. 130, No. 16, 1069–70. **Activity of a New Antimalarial Agent, Chloroquine (SN 7618). Statement approved by the Board for Coordination of Malarial Studies.** [Loeb, R. F., Chairman.]

Chloroquine (SN 7618) is 7-chloro-4-(4 diethylamino-1-methylbutylamino) quinoline, and was synthesized in the United States. It has proved active in various avian malarial infections and in human malaria due to *P. vivax* and *P. falciparum.* Numerous studies have been made during the past two years of its pharmacology and toxicology in man and animals. It is readily absorbed from the alimentary tract, and slowly excreted. A high concentration of the drug is found in organs and tissues after administration, especially in nucleated cells and also in leucocytes, and may greatly exceed that in plasma. In general, its properties resemble those of quinacrine (mepacrine). Like the latter, it is broken down in the body, only 10–20 per cent. of it being excreted unchanged in the urine. Because of its properties, a loading dose should be administered if a high plasma level is to be reached quickly. In experimental animals, the toxicity of this new drug is similar to that of quinacrine. In man, mild transient headache, visual disturbances, pruritus and gastro-intestinal upset have followed doses adequate for clinical treatment of malaria. A regimen of 0·5 gm. weekly, administered to 31 subjects over a period of 11 months, which was above the dose required for suppression, has been well tolerated, except that one subject had an eruption resembling lichen planus, probably due to the drug. It was more active than quinacrine against three types of avian malaria, but like the latter was not curative in these infections, nor did it act as a true prophylactic. In benign tertian malaria it was effective as a suppressant and in the acute attack, but failed as a curative or prophylactic agent. It was also effective in acute attacks of malignant tertian malaria and could effect radical cure. While possessing about three times the activity of quinacrine, it did not colour the skin. A dose of 0·3 gm. on the same day each week proved adequate for suppression. In acute attacks a dose of 0·6 gm. followed by 0·3 gm. after 6–8 hours and one dose of 0·3 gm. on each of two consecutive days caused disappearance of symptoms, freed the blood from parasites, and, in the case of *P. falciparum* malaria, effected radical cure. A total dosage of 1·2 gm. over 24 hours has also proved effective in treatment.

J. D. Fulton.

Work, T. S. **The Synthesis of Antimalarial Compounds related to Niquidine. Part I. Model Experiments on the Synthesis of Quinolyl Carbinols.** *J. Chem. Soc.* 1946, Mar., 194–7.

Work, T. S. **The Synthesis of Antimalarial Compounds related to Niquidine. Part II. Synthesis of a Dihydro-*x*-niquidine.** *J. Chem. Soc.* 1946, Mar., 197–200.

Duncan, G. G. **Quinacrine Hydrochloride as a Malaria-Suppressive Agent for Combat Troops.** *War Medicine.* Chicago. 1945, Nov.–Dec., v. 8, No. 5, 305–18, 7 figs.

In August 1943, the U.S. Sixth Army Training Centre was organized in Australia, to receive from combat units in New Guinea men infected with malaria and to rehabilitate them for further combat duty. The Centre was instructed to try to find improved methods for the treatment and suppression of malaria. Quinacrine [mepacrine] as used up to that date had given disappointing results ; as a suppressive agent it seemed to have failed, and many believed the drug to be actually injurious.

The Centre was situated in a place with a dry, hot climate, the atmospheric temperature not infrequently reaching 108°F. During the first three weeks

of the soldiers' stay, they were put on light duty. During the second three weeks, general camp fatigues, calisthenics, drill, marches and competitive sports occupied their time. During the final four weeks, there was intensive training, simulating as closely as possible the physical demands of combat. Throughout their stay the soldiers received mepacrine in varying doses, with the object of determining the optimum dosage for suppression in combat conditions. Altogether, 3,499 men in four battalions were treated in the initial studies. The men's rations were exceptionally liberal.

An adequate summary of this admirably documented report is not possible, and it should be read in original. Mepacrine was shown to be effective in preventing clinical attacks of malaria among men undergoing most arduous training under combat conditions. Doses of 0·1 gm. daily, six days a week, secure plasma concentrations between 10 and 30 micrograms per litre, with an average of 22 micrograms. Such concentrations prevent clinical attacks, but they are considered an irreducible minimum ; the omission of an occasional dose may permit a clinical attack in persons infected with *P. vivax*. Doses of 0·5 gm. twice a week, at three and four-day intervals, were highly effective. Field observations on a regiment receiving 0·4 gm. twice a week showed equally successful results. A similar degree of protection was not given by 0·3 gm. twice a week. Recurrent attacks of malaria reappeared from two to four weeks after the cessation of suppressive therapy with a frequency equal to that which had preceded three months' intensive suppression. Prolonged administration of mepacrine did not lessen the protection afforded.

It was concluded that the success of mepacrine in suppressing malaria is determined by the thoroughness with which its administration is supervised. Given such supervision, 0·1 gm. daily, 6 days a week, is sufficient ; under combat conditions, when control of administration may be difficult, 0·4 gm. twice weekly, at three- and four-day intervals alternately, is held to be the optimum dosage. *Norman White.*

THOMPSON, A. W. S. **Malaria Control in Mobile Warfare. Italian Campaign 1943-1945.** *J. Roy. Army Med. Corps.* 1946, Mar., v. 86, No. 3, 109–26, 3 figs.

It is the author's contention that " when the Eighth Army landed in Sicily its conception of malaria prophylaxis was not two steps ahead of the previous war " ; nevertheless, by the close of the Italian campaign " the control of malaria in mobile warfare had emerged as a practical proposition for the first time in military history." Mepacrine, standardized pyrethrum insecticides, a pyrethrum protective cream, superior to the old citronella cream [and paris green], were supplied to the Army, but were insufficiently utilized, owing to inadequate planning following the exclusion of hygiene officers from planning arrangements, inadequate training and inadequate appreciation of the risk by combatant officers. In consequence, the Army in Sicily suffered malaria casualties which amounted over a month to 0·88 cases per thousand per day or, if all undiagnosed fevers are included, 1·24 per thousand per day.

In the following year the organization was improved, power sprayers for insecticides and DDT became available, and aircraft for larvicidal work were brought into use, though the value of aircraft for this purpose is questioned. Equally important, the training of troops was improved so that many became conscious of the risk and competent to take individual precautions. In 1945 very elaborate arrangements were made for malaria control work following the Army's break into the Plains of Lombardy, but their effectiveness could not be properly judged owing to the speed with which that offensive brought the Italian campaign to an end.

The result of these improvements is shown in the morbidity statistics. In 1943 the highest weekly peak of malaria incidence was equivalent to an annual rate of 410 cases per thousand. In 1944 the corresponding peak rate was 151 per thousand, and in 1945, up to the end of June, it was 39 per thousand.

The paper has several illustrative examples, including a detailed account of an outbreak in a Division which failed to take adequate precautions when it detrained at a very highly malarious station. The final illustration of the standard reached shows that the malaria casualties in a Corps at the highly malarious station of Venezia Giulia were no more than those in a Corps in a non-malarious station in Austria.

[The author has an interesting story which is very much to the credit of some individuals and organizations, very much to the discredit of others. It does not seem to the reviewer to set out the relevant facts adequately, or in a sufficiently dispassionate manner, for the reader to form an independent opinion on controversial subjects.] *G. Macdonald.*

KNOWLES, F. L. & SMITH, C. S. **DDT Residual House Spray—a Method of Malaria Control in Rural Areas.** *Pub. Health Rep.* Wash. 1945, Oct. 26, v. 60, No. 43, 1274–9.

As a test of the practicability of mosquito control by the use of DDT, an area of 36 square miles, containing 545 houses occupied by plantation negroes on a low standard of living was chosen, and 513 houses were treated with DDT, the remainder being left as controls. Power-driven spray apparatus was used, and the stock solution consisted of DDT 23 per cent., xylol 71 per cent. and Triton X-100 6 per cent., diluted with water to give emulsions of final strength of 5, 2½ and 1 per cent. DDT. The 5 per cent. emulsion gave an actual dose of 64 mgm. per square foot, and presumably the other two doses of 32 and 12 mgm. per square foot.

The full cost of the work is not stated. Material and labour costs for each house amounted to 74 cents, while transport, overhead and other charges had to be added to this, but the total cost per house was probably less than one dollar.

Efficiency of the insecticide was judged by counts of the numbers of *Anopheles quadrimaculatus* in treated and untreated houses. Spraying was completed by August 14, and the percentage reduction in treated houses was :—

	5 per cent. DDT	2½ per cent. DDT	1 per cent. DDT
August 15 to September 15	97	85	63
September 15 to October 14	88	74	66
August 15 to October 14	94	81	66

G. Macdonald.

See also the papers by SIMMONS and his colleagues on the use of DDT in mosquito control (below, p. 789).

GIGLIO, C. L'eradicazione della malaria in Italia. [**The Eradication of Malaria in Italy.**] *Riv. di Malariologia.* 1946, Feb., v. 25, No. 1, 31–5. English summary (3 lines).

BISHOP, Ann & GILCHRIST, Barbara M. **Experiments upon the Feeding of *Aëdes aegypti* through Animal Membranes with a view to applying this Method to the Chemotherapy of Malaria.** *Parasitology.* 1946, Jan., v. 37, Nos. 1/2, 85–100, 2 figs. [25 refs.]

This paper records the results obtained from a continuation of the investigation previously reported by these authors [this *Bulletin*, 1945, v. 41,

731], the object of which was "to obtain sporozoites free from all trace of glandular tissues in order to test the action of drugs directly upon them." It can be seen from the summary of their paper quoted below that the authors have succeeded in this object, and the technique they describe should be of considerable value in obtaining viable sporozoites free from glandular tissue. Later in the paper the authors state: "A complete knowledge of the mode of action of any antimalarial drug which had been proved to eradicate sporozoite-induced infections in experimental animals would involve a study of its action upon sporozoites *in vitro* and upon the primary tissue phase in culture. By such *in vitro* methods it would be possible to compare the action of a drug upon the sporozoites and primary tissue phase of the species of malaria used in the experimental animal (*e.g.*, *Plasmodium gallinaceum* in chicks) with its action upon the sporozoites and primary tissue phase of any of the species of *Plasmodium* of man. In order to approach such a study it is essential that a method should be devised whereby sporozoites can be obtained free from gland tissue and bacterial contaminants. The method in general use whereby sporozoites are obtained for injection is by dissecting out the infected glands from the mosquito and teasing them apart or grinding them up. Such a method is laborious, and though suitable for infection experiments is unsuitable for the study either of the direct action of drugs upon sporozoites or for tissue culture, for it is impossible to ensure that all the sporozoites are free from traces of tissue, and bacterial contaminants may be present." [With this statement the reviewer is in complete agreement, but, whereas the technique described by Bishop and Gilchrist is admirably adapted to fulfil the first requirement, *viz.*, freedom from gland tissue, it does not appear to solve the second problem, that of obtaining sporozoites free from bacterial contaminants, since the feeding mosquito, not being sterile, will presumably introduce them when piercing the membrane with its proboscis.]

During the course of their investigation of the ejection of sporozoites by *Aëdes* in the act of feeding, the authors made a series of other interesting observations which add considerably to our knowledge, not only of the optimum temperature at which the food should be offered, but also as regards how its nature and manner of presentation determine whether it is passed directly into the stomach or first into the diverticula.

The authors summarize their findings as follows:—

"1. Membranes prepared from chicken skin provide a suitable medium through which *Aëdes aegypti* females may be induced to gorge.

"2. Under suitable conditions the proportion of female *A. aegypti* which will gorge through membranes, though more variable than when a living chick is offered, is great enough for experimental purposes.

"3. It is shown that the gorging reaction in *A. aegypti* is provoked by a heat gradient between the environment and the food-limiting membrane.

"4. The feeding reactions of *A. aegypti* towards whole blood, fractions of blood, and other substances have been studied. It was found that (*a*) whole blood, and red corpuscles in saline *when ingested through membranes* go directly into the stomach which becomes fully distended; (*b*) haemoglobin in plasma or distilled water is ingested to a lesser degree than whole blood or red corpuscles in saline, and plasma alone is rarely ingested, but all these pass to the stomach; (*c*) sweet solutions containing glucose or honey are seldom imbibed through membranes and pass to the stomach or diverticula, but only the diverticula are fully distended.

"When offered as *open drops* (*a*) blood is seldom ingested, but if ingested passes to the stomach; (*b*) haemoglobin in plasma or water, or plasma alone, are very rarely ingested, but pass mainly to the stomach; (*c*) sweet solutions

containing honey or glucose, or mixtures of blood and honey are readily ingested and pass mainly to the diverticula which become fully distended, though traces may be found in the stomach.

"5. *Aëdes aegypti* may be infected with *Plasmodium gallinaceum* by allowing them to gorge on drawn infected chicken blood through a membrane. Infection rates comparable to those obtained when the mosquitoes are fed directly on living chickens may be obtained by this method.

"6. If infected mosquitoes are allowed to gorge upon uninfected blood through membranes they eject viable sporozoites into the blood. When young chicks are injected intravenously with blood so infected, infections are produced which in period of incubation and intensity are comparable with those resulting from the bites of infected mosquitoes.

"7. The ejection of sporozoites through membranes in this manner provides a ready means of obtaining sporozoites free from glandular tissue.

"8. Sporozoites collected by this method will be suitable for *in vitro* experiments upon the action of drugs on sporozoites, and also as a source of material for studying in tissue cultures the developmental stages of the malaria parasite arising directly from the sporozoite." *R. M. Gordon.*

DAVEY, D. G. **The Use of Avian Malaria for the Discovery of Drugs Effective in the Treatment and Prevention of Human Malaria. I. Drugs for Clinical Treatment and Clinical Prophylaxis.** *Ann. Trop. Med. & Parasit.* 1946, Apr., v. 40, No. 1, 52–73, 2 charts. [10 refs.]

This paper describes the tests used in the search for new drugs for the clinical treatment of malaria. Earlier descriptions were given by CURD, DAVEY & ROSE [this *Bulletin*, 1946, v. 43, 394]. The tests were made in chicks infected with *P. gallinaceum* or *P. lophurae* and in canaries infected with the latter parasite or *P. cathemerium*. Briefly, they were as follows. After intravenous infection of the host with a standardized number of parasites, oral treatment with the drug was given once on the day of infection and twice daily thereafter for 3–4 days. The degree of parasitaemia in control and treated birds was then compared at the time (about the 5th day) when the infection in the former had reached its peak. Mepacrine was used as the standard drug, and all conditions such as type and weight of bird, size of inoculum and method of dosage were strictly controlled.

The activity of the drug was assessed by noting the critical dose region obtained from a dose-response curve constructed over the usual period of administration. "The upper limit of this region is approximately the lowest dose of the substance exerting what is materially its maximum effect; the lower limit is approximately the lowest dose exerting a measurable effect." The upper limit was regarded as the minimal effective dose (M.E.D.) of the substance which produced uniformly low parasite counts in the treated birds. At first the results obtained with *P. gallinaceum*, and the toxicity of a drug for mammals, served as guides to its possible value in human malaria. The distribution of a drug in the body of the host was in some cases studied by chemical analysis. Additional information on its rate of absorption was given by comparing the acute oral and corresponding intravenous toxicity. In order to study the manner in which the host deals with the drug when variation in the rate of absorption is excluded, rapid intravenous injection was employed. The study of the direct action of drugs on the parasites is projected.

The activity of different drugs in infections following their intravenous, as opposed to oral administration, was also investigated. Approximate values for the rates of absorption of certain drugs relative to that for mepacrine, their activity in avian malaria when given by the oral and intravenous routes, as

well as their activity in human malaria, are recorded in tabular form. The conclusion is drawn that the intravenous test gives a better indication of the dose necessary for the treatment of human malaria. By using different types of infection, considerable specificity of action was discovered, which adds to the difficulty of test. As a check on specificity of action American workers always carry out tests on more than one species of plasmodium, and the same course has been followed in the present investigation. When testing against various species, differences in physiology of the host have been avoided by infecting it with different plasmodia where possible. Details of the methods should be consulted in the original. It appears that when canaries infected with *P. cathemerium* are used, the author's results are easier to interpret than those obtained by the Roehl technique. The steps adopted in selecting a drug for clinical trial are outlined. *J. D. Fulton.*

BRACKETT, S., WALETZKY, E. & BAKER, Margaret. **The Rate of Action of Sulfadiazine and Quinine on the Malarial Parasite** *Plasmodium gallinaceum.* *J. Pharm. & Exper. Therap.* 1945, July, v. 84, No. 3, 254–61, 2 figs. [13 refs.]

Chickens infected with *P. gallinaceum* by blood inoculation were treated continuously with large amounts of quinine or sulphadiazine in order to compare the rate of activity of the two drugs. It was found that quinine acted almost immediately, in most cases arresting the development of the parasites entirely. In one bird only nuclear division in the young schizont proceeded to the four-nuclear stage. In the case of sulphadiazine the first detectable retardation of development occurred between the 12th and 24th hours. The first treated generation of parasite proceeded to segmentation, the liberated merozoites entering other erythrocytes. These young parasites were unable to develop beyond the four-nuclear stage. It was also observed that though the first generation proceeded to schizogony, the average number of merozoites produced was 12·7, compared with 20·3 in the controls. As a result of this difference in rate of action of the two drugs, in chickens treated with quinine there was never any increase in the number of parasites in the blood, whereas with sulphadiazine there was a four-fold increase during the first two days. In the controls the increase was fifteen-fold. It is suggested that in the case of slowly acting drugs like the sulphonamides, the rate of action runs parallel to the rate of growth of the organism. *C. M. Wenyon.*

FUNKE, A., BOVET, D. & MONTÉZIN, G. Quinoléines à chaine latérale arylaliphatique douées de propriétés antimalariques. [**Quinoline Derivatives with Aliphatic-Aromatic Side Chains having Antimalarial Properties.**] *Ann. Inst. Pasteur.* 1946, Mar.–Apr., v. 72, Nos. 3/4, 264–74, 1 fig.

Many substances have been synthesized on the model of plasmoquine (quinoline nucleus) and on that of mepacrine (acridine nucleus), in which the ring systems or basic side chains have been altered. It appears that the latter have no specific action but are necessary for antimalarial activity. The present authors, by condensation of 6-methoxy-8-aminoquinoline with the halogen derivative prepared from the aliphatic-aromatic amino alcohol $OH.CH_2.C_6H_4.CH_2.N(C_2H_5)_2$ have obtained 4′-diethylaminomethyl-8-benzylamino-6-methoxy quinoline (2236F) in which the side chain is of a novel type. The corresponding primary amine and next higher homologue were also prepared as well as the *ortho-* and *meta*-isomers, besides compounds with two substituent methyl groups in the aromatic ring. In the acridine series two analogous derivatives were prepared. Antimalarial tests were carried out in the usual way on canaries

infected with *P. relictum*, the drug being given subcutaneously. All but one compound of each series showed activity. The most active was 2236F with a chemotherapeutic index of 1/50. Its toxicity was low and the authors believe that it merits clinical trial. *J. D. Fulton.*

ZAIN, H. Malariaimmunität und Rezidiventstehung unter Berücksichtigung der Endothelstadien (*Plasmodium gallinaceum*). II. Mitteilung. [**Immunity and Relapse in regard to the Endothelial Stages of** *P. gallinaceum.*] *Deut. Tropenmed. Ztschr.* 1944, Apr.–May, v. 48, Nos. 7/10, 156–68, 2 figs. [19 refs.]

The author has shown that the serum of latently infected chickens which have been subjected to repeated injections of chicken blood heavily infected with *P. gallinaceum* contains antibodies in sufficient amount to give rise to a passive immunity in chickens which have been injected with it. This passive immunity is exemplified by the delay in the appearance of parasites in the blood after inoculation, and the lowering of the intensity and the curtailment of the resulting infection. When such immunized chickens are subjected to superinfection, not only is there a failure of parasites to appear in the blood, but there is also no new development of exoerythrocytic forms. Similarly, when a blood relapse is caused by splenectomy, this is not associated with the reappearance of exoerythrocytic forms. It seems clear, therefore, that the immune bodies in the serum are directed against both the erythrocytic and exoerythrocytic stages of the parasite. The question arises as to whether there is only one immune body capable of checking the development of both stages of the parasite, or whether two distinct bodies are involved.

To settle this question, an attempt was made to liberate into the blood stream any immune bodies which might exist in the reticulo-endothelial cells, and which might be supposed to be immune bodies having a special action on the exoerythrocytic stages which develop in these cells. Accordingly, chickens with latent malarial infection, whose blood serum was shown to be devoid of any immunizing properties, were subjected to repeated injections of manganese chloride. This had the effect of conferring on the blood immunizing properties which it did not previously possess, as a result, it is concluded, of the liberation of immune bodies from the reticulo-endothelial cells. These properties differed in no way from those possessed by the serum of chickens immunized by the repeated injection of heavily infected blood as in the first experiments. It seems clear, therefore, that the immune bodies produced by the stimulus of erythrocytic forms of the parasite are not different from those appearing in endothelial cells under the stimulus of the exoerythrocytic stages of development. As exoerythrocytic forms occur in the endothelial cells of the blood vessels as well as in cells of the reticulo-endothelial system in the tissues, the further question arises :—are the parasites in these two situations identical as regards their susceptibility to the immune substances in the blood, or are there differences between them which might have some bearing on the fact that sporozoite-induced malaria in man is liable to repeated relapse while blood-inoculated malaria is not ? *C. M. Wenyon.*

WOLFSON, Fruma. **Effect of Preservation by Freezing upon the Virulence of Plasmodium for Ducks.** *Amer. J. Hyg.* 1945, Sept., v. 42, No. 2, 155–66.

The paper describes the results of experiments designed to test the degree of survival of three species of avian malarial parasite (*P. cathemerium*, *P. lophurae* and *P. relictum*) when blood taken from infected ducks is subjected to rapid freezing and, following storage at −76°C. for periods varying from two hours to

one year, to rapid thawing at 42°C. The effect of these procedures was estimated by the study of Giemsa stained films of the stored blood and by the results of inoculation into young ducks. It was found that the proportion of erythrocytes and probably of parasites which survived varied directly with the proportion of parasitized erythrocytes in the sample of blood before freezing. This is contrary to the findings of MANWELL and EDGETT in similar experiments. They stated that the greater the number of parasites in the blood the greater was the proportion of erythrocytes destroyed [this *Bulletin*, 1944, v. 41, 189]. The author of the present paper found that the preservation of *P. cathemerium* had no effect on the length of the prepatent period, the day on which the peak of parasitaemia occurred and the degree of the parasitaemia at the peak. The three parasites investigated showed no appreciable differences in their ability to survive, as judged by the number of erythrocytes and parasites surviving, but the results of the infectivity tests indicated that *P. cathemerium* survived more regularly than the other two parasites. It was noted that ducks inoculated from those infected from the frozen material developed a lower degree of parasitaemia than did controls, but that from one to three subsequent passages were usually sufficient to restore the virulence of the parasite. *C. M. Wenyon.*

MARVIN, H. N. & RIGDON, R. H. **Terminal Hypoglycemia in Ducks with Malaria.** *Amer. J. Hyg.* 1945, Sept., v. 42, No. 2, 174–8, 2 figs. [12 refs.]

A study of the blood sugar level in ducks infected with *Plasmodium lophurae* has shown that there is an increasing hypoglycaemia following the peak of infection. At the time of death, usually 8 hours after the peak, there may be a 60 per cent. reduction in the blood sugar. As malarial parasites require relatively large amounts of sugar for their development *in vitro*, it seems reasonable to suppose that the fall in the parasitaemia is the direct result of the hypoglycaemia. This is supported by the observations made by HEGNER and MACDOUGALL [this *Bulletin*, 1926, v. 23, 863] that a hypoglycaemia caused by injections of insulin brought about a decrease of malarial parasites in canaries. According to the authors, the course of events in these malarial infections in ducks is an anaemia caused by destruction of erythrocytes, leading to anoxaemia. This damages the liver, with impairment of hepatic function and hypoglycaemia, which contributes to the death of the host in spite of the fact that it brings about a decrease in the parasitaemia. *C. M. Wenyon.*

RIGDON, R. H. *Plasmodium lophurae* **Infection of the Chick Embryo.** *Amer. J. Hyg.* 1945, Sept., v. 42, No. 2, 189–94.

The author has studied the results of inoculation of *Plasmodium lophurae* from infected ducks and chicks into developing chicken eggs. The results indicate that infection will not occur in embryos when infected blood is injected into the yolk sac. Infections, on the other hand, will result if the blood is inoculated directly into the embryo. If such inoculated embryos are allowed to hatch, it will be found that usually few if any parasites are present in the blood. In only one chick was there a high grade parasitaemia at the time of hatching. More often parasites first appeared in the peripheral blood on the third or fourth day after hatching and the degree of the resulting parasitaemia varied. Some chicks showed only a few parasites on several days while others developed a high degree of parasitaemia. It appears from this study that the chick embryo is not such a suitable host for *P. lophurae* as the young chick. Some unknown factor in the embryo appears to hinder its development. No significant pathological lesions were observed in the infected embryos except

splenic enlargement and some pigment in the spleen and liver. No exoerythrocytic forms of the parasite were found. *C. M. Wenyon.*

WOLFSON, Fruma. **Virulence of the IG Strain of *Plasmodium relictum* for the Duck.** *Amer. J. Hyg.* 1945, Sept., v. 42, No. 2, 111–18, 2 pls. [12 refs.]

A strain of *Plasmodium relictum* sent from England to America in canaries was inoculated to young ducks. At first it produced only mild infections, but after 40 semi-weekly transfers it had increased in virulence to such an extent that the standard dose (3 billion [=3,000 million] parasites per kilogram of body weight) caused some deaths, which occurred usually within the first week of inoculation. It is clear that rapid passage through a new host is a satisfactory method of adapting a parasite to residence in a host only slightly susceptible on the first transfer. *C. M. Wenyon.*

TRYPANOSOMIASIS.

DE AZEVEDO, J. F., CAMBOURNAC, F. J. C. & PINTO, M. R. Sobre as preferências hemáticas das Glossinas da Guiné. [**The Blood Preferences of *Glossina* in Portuguese Guinea.**] *An. Inst. Med. Trop.* Lisbon. 1945, Dec., v. 2, 67–74. English summary.

KARTMAN, L., CAMPAU, E. J., NEWCOMB, E. H. & MORRISON, F. D. **A Note on the Noise-making Ability of the Tsetse-Fly, *Glossina palpalis* Rob.-Desv. (Diptera, Glossinidae), while in Flight.** [Research Notes.] *J. Parasitology.* 1946, Feb., v. 32, No. 1, 91.

While collecting *Glossina palpalis* in French West Africa in 1944 and 1945 the authors noticed that the fly had " a rather noiseless flight during the early morning hours when the air was relatively cool," but as the air became warmer the fly made " a very distinct and characteristic buzzing noise " which was loudest during the noonday and afternoon heat. BEQUAERT's statement in the report of the Harvard-African expedition to Liberia and the Belgian Congo [see this *Bulletin*, 1931, v. 28, 258] that the flight of *G. palpalis* is noiseless is quoted and it is suggested that there may be physiological differences between the flies of the two regions. *J. F. Corson.*

WIEN, R. **Chemotherapeutic Action of Amidine and Phenanthridinium Compounds in *T. congolense* Infections.** *Brit. J. Pharmacol.* 1946, Mar., v. 1, No. 1, 65–80, 3 figs. [24 refs.]

The author has studied the therapeutic action of 19 diamidines and 9 phenanthridinium compounds on *T. congolense* infections in mice ; the diamidines comprised 12 of the stilbene, 4 of the diphenoxy, and 3 of a miscellaneous series. Special attention was given to No. 897 (7-amino-9-*p*-aminophenyl-10-methylphenanthridinium chloride) and to No. 991 (4 : 4′-diamidino-αβ-dimethylstilbene dihydrochloride), which had previously been compared with one another by FULTON and YORKE [this *Bulletin*, 1943, v. 40, 19] and by CALVER [this *Bulletin*, 1945, v. 42, 704]. Also specially studied was No. 1553

(2 : 7-diamino-9-phenyl-10-methylphenanthridinium bromide), which has given particularly promising results in the field [first reported by CARMICHAEL and BELL, this *Bulletin*, 1945, v. 42, 259].

The more important compounds were tested against five *T. congolense* strains, comprising 2 of the chronic and 3 of the acute type. The two chronic strains are stated to be probably derived from a common parent stem, *i.e.* Strain I of Calver [*loc. cit.*]. [It is not stated that the three acute strains were also all derived from a common stem, Calver's Strain II ; one came from the Liverpool School of Tropical Medicine, where it had been received in 1937 from the Wellcome Bureau of Scientific Research, to which it had previously been given by Professor C. H. Browning ; the other came from Dr. F. Hawking, who had received it in 1942 from the Liverpool School of Tropical Medicine.]

Certain of the author's results proved to be at variance with those reported by BROWNING and CALVER [this *Bulletin*, 1945, v. 42, 259] and CALVER [*loc. cit.*]. Thus, the latter investigators had found Phenanthridinium 897 to be curative for Strain I at about one-tenth of the dose required for Strain II infections ; Wien, however, found the curative doses to be about the same. Again, Calver had found Diamidine 991 to be considerably less effective than Phenanthridinium 897, but Wien (confirming FULTON and YORKE, this *Bulletin*, 1943, v. 40, 19) found the therapeutic indices for these compounds to be about the same ; in fact, against one of the chronic strains, 991 had a slightly higher therapeutic index than 897 (the difference was statistically not highly significant).

Phenanthridinium 1553 was confirmed as an outstanding compound, with an index of 152, as compared with an index of 10 for Phenanthridinium 897 and 12 for Diamidine 991, when tested against one of the acute strains.

There is a discussion on the relationship between chemical structure and *T. congolense* activity, which should be read in the original by those interested. The author's own summary of this relationship is as follows :—

" *Diamidine Compounds*

" (*a*) The introduction of methyl groupings into the unsaturated stilbene linkage enhanced activity ; nuclear substitution was not so effective.

" (*b*) Nuclear substitution by various groupings in the 2-position did not increase activity, except for a slight effect with methyl, amino and acetamido derivatives, although it was found that the introduction of halogen markedly increased activity against *T. equiperdum* (results to be published). Alkyl substitution in the amidine grouping and substitution of a diphenylamine for the stilbene linkage were without effect.

" (*c*) The comparatively high activity of phenanthrene-3 : 6-diamidine was of interest. An analogous compound, 3 : 6-diamidinocarbazole, was devoid of activity.

" *Phenanthridinium Compounds*

" (*a*) The replacement of amino by amidine groupings resulted in loss of activity.

" (*b*) The substitution of the 9-(3′-aminophenyl) by the 9-(3′-pyridyl) grouping led to a reduction in activity. [Abstracter's note : For " 9-(3′-aminophenyl)" the author presumably intended " 9-(4′aminophenyl)"].

" (*c*) The introduction of an unsaturated linkage (*p*-dimethylaminostyryl) between phenyl at C 9 and the phenanthridine nucleus also led to a reduction in activity."

The author has also investigated some of the pharmacological properties of Phenanthridinium 1553. He summarizes his conclusions by the statement that, in general, it has a depressant action on the circulation and respiratory centre, and in high doses, a toxic action on the liver and kidneys.

E. M. Lourie.

MARTINS, A. V., VERSIANI, V. & TUPINAMBÁ, A. A. Estudos sôbre a moléstia de Chagas no estado de Minas Gerais. I. Estudo epidemiológico de um foco da moléstia no município de Jaboticatubas. [**Chagas's Disease in the State of Minas Geraes. I. Epidemiological Study of a Focus in Jaboticatubas.**] *Arquivos do Inst. Químico-Biol. Estado de Minas Gerais.* 1945, v. 1, 51–61, 12 figs. on 9 pls. English summary (10 lines).

This investigation was carried out at the end of 1939 and the beginning of 1940 and was cut short by the death of Evandro Chagas. Jaboticatubas is a small municipality in central Minas Geraes, some 70 kilometres from the capital. The inhabitants live in hovels (*cafuas*), some with mud walls, made of woven twigs and laths, the interstices being filled with earth, others with unceiled tile roofs. The district is fairly dry and relatively healthy; there is no malaria, but infestation with *Ascaris lumbricoides* is very common. The inhabitants live by cultivating millet and manioc, and, to a small extent on the lower levels, rice.

Of 18 mud huts investigated, 15 were harbouring the vector of *T. cruzi*, and the insects were found infected in 9 of them. Only one of the tiled huts was infested and the insect caught was positive for *T. cruzi*. Of a total of 146 inhabitants, 33 were found positive by examination of thick drops and by xenodiagnostic methods. In 10 of the 18 mud huts the inhabitants were positive, and in 7 of the tiled huts. In the former the inhabitants totalled 102, and 23 of them were infected; in the latter 44, and 10 were infected. Of the 33 infected, 15 were in the second decade; none was under one year of age. There was no appreciable difference as regards sex; 14 of 66 males were infected and 19 of 80 females.

Animals were also examined. Of the domestic animals, 5 of 22 dogs and 2 of 7 cats were infected; all 7 were in the mud huts, none in the tiled. Forty wild animals belonging to 9 species were examined, but only two armadillos (*Dasypus novemcinctus*) were positive. Of 124 *Panstrongylus megistus* examined 36 were positive, and 7 of 51 *Triatoma sordida*, that is, 43 were positive out of a total of 175 vectors examined. There are 12 photographs showing clearly the terrain and the inhabitants. *H. Harold Scott.*

MARTINS, A. V., VERSIANI, V. & TUPINAMBÁ, A. A. Estudos sôbre a moléstia de Chagas no estado de Minas Gerais. II. Sôbre 156 xenodiagnósticos feitos em Belo Horizonte. [**Chagas's Disease in the State of Minas Geraes. II. One Hundred and Fifty-Six Xenodiagnostic Tests carried out in Belo Horizonte.**] *Arquivos do Inst. Químico-Biol. Estado de Minas Gerais.* 1945, v. 1, 63–70, 1 folding map. English summary.

Xenodiagnosis has proved to be the most reliable test in chronic cases of Chagas's disease. The subjects selected for the test were attending the hospitals and clinics in Belo Horizonte, Minas Geraes, Brazil. The investigation was carried out at intervals between April 1939 and August 1942, and the subjects chosen came under one or other of four categories: i. With myocarditis of undetermined cause. ii. With mal de engasgo (mega-oesophagus) [see this *Bulletin*, 1921, v. 18, 301; 1927, v. 24, 830]. iii. With goitre, with or without cretinism. iv. Those with no definite symptoms, but presenting themselves for examination either because they lived in places where Chagas's disease is endemic, or because others of their families were suffering from it.

The insects used were *P. megistus*, *T. infestans* and *T. vitticeps*, reared in the laboratory. They were examined 40 days after their feeding on the patient; their rectal contents taken by pipette and later their whole bodies were dissected and examined.

Generally, one test only was made with each patient. The results were as follows: Of 63 in Group i (myocarditis patients) 23 were positive; of 48 in Group ii (mega-oesophagus) 22 positive; of 28 in Group iii (goitre) 5 positive, and all came from parts of the State where infected bugs had been captured. Of Group iv one was positive out of 17. In all, 51 were positive among the 156 tested. The distribution in the 32 municipalities is given, but this is not of much value, since none gave more than 3, and 18 had only one each; 9 had two. *H. Harold Scott.*

VIZCARRONDO R., O. Notas sobre la enfermedad de chagas y en particular en el Estado Aragua. [**Notes on Chagas's Disease, especially in the State of Aragua.**] *Rev. Sanidad y Asistencia Social.* Caracas. 1945, Oct.–Dec., v. 10, Nos. 5/6, 635–66, 1 map & 15 figs. on 10 pls. [41 refs.]

As usual in articles on Chagas's disease the opening pages repeat the history of Carlos Chagas's early work, the vectors of infection and the modes of conveyance. After this, the author shows on a sketch map the places where infected *Rhodnius* were found, but in 7 chief districts only 107 insects were examined; 48 were found positive. Next, examinations were made of inhabitants of the town of Maracay. Eight per cent. of schoolchildren had palpable spleens and 6 per cent. harboured malaria parasites; the corresponding figures for soldiers were 13 and 11 per cent., and for "various people in the town" 4 and 6 per cent. [These figures convey little, if any, useful information since in no case is the number examined stated.] Then follow descriptions of three cases. The first is called "a case of lymphatic leukaemia with leucopenia," seemingly because there was a relative lymphocytosis. Red corpuscles numbered 1,300,000, white 1,600 per cmm., lymphocytes 42 per cent. Ova of *Necator americanus* and of *Trichuris trichiura* were found in the stools and the case would appear to have been one of helminthic infestation with secondary anaemia. Malaria parasites were repeatedly looked for, but in vain. The second was a case of myelocytic leukaemia; the third had some degree of anaemia and xenodiagnosis proved infection by *T. cruzi*. Other "notes" include a chemical analysis of the water of Lake Tacarigua made in 1941, and research on the use of DDT, its pharmacological action and its compatibles.
H. Harold Scott.

LIEM, S. D. & VAN THIEL, P. H. **The Complement-Fixation Test for Chagas' Disease employing a Dried Culture Antigen.** *Acta Leidensia* (*Scholae Med. Tropicae*). 1940–41, v. 15–16, 259–74.

Tests of a dried antigen prepared from a culture of trypanosomes on horse blood glucose agar [see LIEM, this *Bulletin*, 1938, v. 35, 719] are described. The strain of trypanosomes was isolated at Hamburg in 1935 by MALAMOS [*ibid.*, 1935, v. 32, 718] from *Macaca irus* [*Macacus cynomolgus*] recently arrived from the Netherlands East Indies; it was identified by Malamos as *T. cruzi*. The authors received the strain in the bug *Triatoma infestans* in 1936.

The sera of rabbits immunized by intravenous injections of cultures of the trypanosome, and the sera of dogs infected with it, were used for antibody, while guineapig serum provided the complement. The sera of two persons in South America who were suffering from Chagas's disease were sent to the authors at Leiden, Holland, and gave negative results in the complement fixation test, but, owing to the time taken in transit, no conclusion can be drawn from the tests. As a control, 365 sera of patients in Holland, suffering from various diseases, were tested: 4 out of 146 Wassermann-positive sera were positive and 4 out of 6 sera of patients suffering from chancroid were also positive, but all the other sera were negative.

The authors conclude that the dry antigen used, which is sealed *in vacuo* in ampoules and kept in the refrigerator, is better than other antigens, and they recommend its trial in known cases of Chagas's disease in South America.

J. F. Corson.

MAZZA, S., BASSO, G. & BASSO, R. Investigaciones sobre enfermedad de Chagas. Contribución para la terapéutica de la enfermedad de Chagas. Ultimos ensayos quimioterápicos: M.3024, I.C.I. Aplicación de *penicilina.* [**Studies on Chagas's Disease. Treatment with M.3024 and with Penicillin.**] *Universidad Buenos Aires: Misión de Estudios de Patologia Regional Argentina (Jujuy) Publicación No. 70.* 1945. 81 pp., 56 figs. [Bibliography.]

The authors begin by reviewing the literature on the use of 7602 (Ac) Bayer in Chagas's disease, and follow this by a record of cases in which they have used M.3024, the British equivalent of the Bayer preparation. Several of these cases are detailed. The initial dose is 7–12 mgm. per kilo body-weight, usually 0·15 gm.; 2–4 cc. were generally given at 5–7-day intervals, the second dose being double that of the first. Improvement was rapid and the external signs (swelling of the eyelids and face) disappeared in 5–12 days.

Penicillin was then tried. It was given by intramuscular injection, 2 cc. every 3 hours, containing 5,000 Oxford units per cc. Again, several cases are detailed and the total amount given was about 400,000–500,000 units. Both local and systemic symptoms improved. [The authors do not attempt to discuss the relative values of these forms of treatment. It would be instructive if they would present parallel series of cases and a reasoned discussion of the results observed.]

H. Harold Scott.

LEISHMANIASIS.

GEVORKOV, A. A. **Incidence of Visceral Leishmaniasis in Samarkand during 20 Years (1924–1944).** *Med. Parasit. & Parasitic Dis.* Moscow. 1945, v. 14, No. 3, 86–9. [In Russian.]

The author analyses the incidence of visceral leishmaniasis in Samarkand (Middle Asia) from 1924 to 1944. During this period the total number of recorded human cases was 921, which were fairly evenly distributed from year to year, in spite of a progressive increase in the population in the course of 20 years. Thus, the absolute growth of the population was not accompanied by a proportional rise in the incidence of kala azar. A comparison of the figures for the incidence of leishmaniasis in man and in dogs for 11 years (1933–43) shows that there is a complete parallelism between the two diseases, the fluctuation in the incidence of human disease corresponding to that in the canine, and being correlated not only with the percentage of infected dogs but also with the total number of dogs in the town.

As regards incidence in age-groups, the great majority of cases (54–74 per cent. of all cases) occur in children between the ages of one and five, and chiefly from one to three. Children older than ten years are rarely affected, while during the last nine years there has not been a single case of infection in persons older than 18 years.

It is concluded that the stabilization of the incidence of kala azar in Samarkand is due to the systematic measures adopted for the early diagnosis and treatment of the disease, as well as to the elimination of infected dogs. The latter are regarded as constituting the chief epidemiological danger.

C. A. Hoare.

JUNG SUN, C. **Kala-Azar in Lanchow and its Vicinity.** *Chinese Med. J.* (Chengtu Edition.) 1944, Oct., v. 63A, No. 1, 12.

MUNTER, E. J. & PACKCHANIAN, A. **Two Exogenous Cases of Visceral Leishmaniasis (Kala-Azar) in the United States with Notes on Cultivation of *Leishmania donovani* in Vitro.** *Amer. J. Trop. Med.* 1945, Nov., v. 25, No. 6, 507–12, 4 figs. [12 refs.]

The cases reported were in native Indian seamen from Assam, where the disease was contracted. Diagnosis was established by the discovery of leishmania in smears of bone marrow and in cultures made from the bone marrow and the peripheral blood. Various serological tests were also positive.

C. M. Wenyon.

NÁJERA ANGULO, L. Observaciones sobre el ciclo evolutivo de *Leishmania infantum* Nicolle, 1908. [**The Developmental Cycle of** *Leishmania infantum*.] Reprinted from *Rev. Ibérica de Parasit.* Granada. (Tomo extraordinario.) 1945, Mar., 181–98, 1 fig. & 1 coloured pl. [22 refs.]

In this paper the author upholds the view, as others have done, that the parasite of infantile kala azar may reproduce by schizogony. The majority of observers believe, however, that the appearances of schizogony are due to the presence of leishmania in detached portions of the cytoplasm of infected macrophages in which the outlines are not visible owing to bad fixation or degenerative changes. In the present paper the author suggests that certain granular cytoplasmic bodies seen especially in smears of the bone marrow of cases of infantile kala azar, and which contain no semblance of the characteristic leishmania nuclei and kinetoplasts, are actually young schizonts. They are described as increasing in size till they are larger than a red blood corpuscle. Associated with this growth there are gradually formed in the cytoplasm, presumably from the granules, a series of nuclei and kinetoplasts. Finally by separation of cytoplasm around the nuclei and kinetoplasts a varying number of leishmania are formed, which lie in a cyst membrane, the remains of the supposed schizont. These leishmania are liberated by rupture of the cyst, and either commence the process again or are phagocyted by the macrophages. These phagocyted leishmania may fill the macrophages and have hitherto been regarded as parasitic in these cells. According to the author they are destined for phagocytic destruction. What is perhaps most remarkable is the author's opinion that this type of development is peculiar to *Leishmania infantum* and will account for the differences in the diseases caused by this parasite and *L. donovani*. The paper is illustrated by black and white text figures and a coloured plate which the reviewer has to admit he finds unconvincing.

C. M. Wenyon.

ADLER, S. **The Sandflies of Cyprus (Diptera).** *Bull. Entom. Res.* 1946, Feb., v. 36, Pt. 4, 497–511, 6 text figs. & 4 figs. on 1 pl. [24 refs.]

Ten species of *Phlebotomus* were collected in Cyprus during August and September 1944. They were : *P. papatasi*, *sergenti*, *alexandri*, *perniciosus* var. *tobbi*, *chinensis*, *perfiliewi*, *larroussei*, *parroti*, *azizi* sp. n., and *fallax* var. *cypriotica* var. nov.

Taxonomy of these species is discussed and the new forms are described and illustrated ; keys to both sexes are provided.

The incidence of human visceral leishmaniasis in the island is unknown, though the first case was recorded in 1935. Canine kala azar is not rare ; the author considers that *P. perniciosus* var. *tobbi*, and a race of *P. chinensis*, should be investigated as possible vectors.

H. S. Leeson.

CHATTERJEE, H. N. **Postmortem Femoral Bone Marrow Studies of Kala-Azar.** *Trans. Roy. Soc. Trop. Med. & Hyg.* 1946, Feb., v. 39, No. 4, 315–20, 4 figs. on 1 pl. [13 refs.]

An examination of the femoral bone marrow from fatal cases of kala azar has shown that in an acute case there was almost complete absorption and replacement of the fat cells. There was a total absence of the degenerative changes met with in later stages of the disease, the general structure of the marrow being made up of large numbers of clasmatocytes and cells of the myeloblastic series. Of the clasmatocytes about 30 per cent. contained leishmania. In later subacute cases the marrow, reddish in colour, was tougher than normal. The total number of cells was diminished, particularly in certain areas which contained few cells and presented a homogeneous ground-grass-like appearance. Of the clasmatocytes present, nearly all contained leishmania. The ground-glass-like material was the result of precipitation of fine fibrils in the fat vacuoles. In addition there was some increase in the argyrophil reticular fibres. In later chronic cases there was a further reduction in the number of cells, those of the myeloid series being remarkably diminished. The reticulo-endothelial cells of clasmatocytes were the most conspicuous cells. They possessed a large amount of amoeboid and branched protoplasm and were packed with parasites. The fibrils noted in the subacute cases were more pronounced, while there was a marked proliferation of the argyrophil reticular fibres. The author concludes that the progressive degeneration of the marrow, and the cellular changes, will explain the leucopenia and neutropenia and increasing anaemia which are characteristic of kala azar. *C. M. Wenyon.*

GELLHORN, A., VAN DYKE, H. B., PYLES, W. J. & TUPIKOVA, N. A. **Amyloidosis in Hamsters with Leishmaniasis.** *Proc. Soc. Exper. Biol. & Med.* 1946, Jan., v. 61, No. 1, 25–30, 3 figs.

In a recent paper GOODWIN [this *Bulletin*, 1946, v. 43, 318] has shown that hamsters infected with *Leishmania donovani* may suffer from oedema, nephritis, proteinuria and depression of the level of the plasma proteins. The authors of the present paper confirm these findings and give the additional information that, on and after the 46th day of the infection, an increasing degree of amyloidosis occurs in various organs, more particularly in the kidneys and suprarenals. At the same time it was noted that though the globulin level in the blood remained normal, the albumin level fell considerably, so that the A/G ratio was significantly lowered in the infected animals. This decrease in the blood albumin was correlated with the passage through the kidneys of increasing amounts of albumin due to the amyloid degeneration of the glomeruli and to a lesser extent of the tubules. At the same time there was a lowering of the colloid osmotic pressure of the plasma, leading to the escape of excessive amounts of fluid into the tissues and to the development of oedema and anasarca. The authors do not believe that failure of the synthesis of plasma albumin is responsible to any important extent for the lowering of the percentage of this protein in the plasma. *C. M. Wenyon.*

SEN GUPTA, P. C. **4 : 4′ Diamidino-Diphenyl-Ether in the Treatment of Indian Kala-Azar.** *Indian Med. Gaz.* 1945, Oct., v. 80, No. 10, 495–8.

In an earlier communication [this *Bulletin*, 1945, v. 42, 264] the author reported upon the treatment of 16 cases of kala azar with this drug, which has been given the proprietary name of phenamidine (M & B 736). In the present paper these 16 cases, together with 14 others similarly treated, are considered. The ages varied from 1 to 50 years, and the duration of illness from

1 month to 2 years. The drug was administered intravenously in 1 per cent. solution, the usual course being one injection each day for 10 days. This was followed by a second course after a 10-day interval. The initial dose for an adult was 25 mgm. This was increased by 25 mgm. daily till a dose of 1 mgm. per pound of body weight was reached. The mean total dose for an ordinary case worked out at 1·73 gm.±0·477 gm., or for 100 pounds of body weight, 1·854±0·396 gm. Of the 30 patients, 24 completed the treatment and were discharged as clinically cured. Six months later 21 of these were traced. Sixteen were in good health and were considered cured, while five had relapsed. The permanent cure rate is given as 64±19 per cent. It is concluded that the drug is inferior to the most effective pentavalent antimonials or to diamidino-stilbene. On the other hand it is non-toxic and should be useful in cases in which antimonials are contraindicated as, for instance, when the complication of grave pulmonary tuberculosis exists. *C. M. Wenyon.*

WIEN, R. **Excretion of Stilbamidine.** *Trans. Roy. Soc. Trop. Med. & Hyg.* 1946, Apr., v. 39, No. 5, 455–8.

Stilbamidine was injected subcutaneously into rats in doses of 1 to 10 mgm. per kgm. every day for 15 days, and the excretion in the urine was measured by means of the fluorescence (which measures the unchanged molecule) and by a glyoxal reaction (which measures both the unchanged and slightly changed molecule). With a daily dose of 1 mgm. per kgm. the percentage excretion of the day's dose was 1·6 on the 5th day, 1·8 on the 10th day, and 2·5 on the 15th day when measured by the fluorescence, and 42 on the 5th day, 52 on the 10th and 59 on the 15th day when measured by the glyoxal method. A large proportion of stilbamidine was presumably metabolized and excreted in a non-fluorescent form. Similar results were obtained when the excretion of 2-amino 4 : 4′diamidino-stilbene was studied; this compound is closely similar to stilbamidine (4 : 4′diamidino-stilbene) but it can be estimated by diazotization as well as by fluorescence. The greater the number of injections of stilbamidine which had been given, the higher was the proportion of the daily dose excreted. Conversely, the larger the daily dose, the smaller was the proportion excreted; presumably the kidney could eliminate only a limited amount of the compound. The higher doses (5–10 mgm. per kgm.) were toxic, and some of the animals died. *F. Hawking.*

PACKCHANIAN, A. **Leishmaniasis. The Cultivation of *Leishmania tropica* from Two American Soldiers who had returned to the United States from the Near East.** *J. Amer. Med. Ass.* 1945, Oct., 20, v. 129, No. 8, 544–7. [Refs. in footnotes.]

The paper is based on two cases of oriental sore in soldiers returned to the U.S.A. from Iran. In both cases parasites were demonstrated in the lesions, while cultures in the water of condensation of blood agar medium were obtained. Attention is called to this occurrence of exogenous cases of oriental sore in the U.S.A. and a warning is issued that further cases of the kind may be expected. The author advises the making of cultures in all suspected cases, for if a positive culture is obtained there is no danger of confusing the flagellates with other organisms, whereas in smears from the sore inexperienced observers may confuse yeasts with leishmania and in consequence make an erroneous diagnosis. *C. M. Wenyon.*

KOJEVNIKOV, P. V. [**The Absence of Cross-Immunity between the Two Types of Cutaneous Leishmaniasis.**] *Med. Parasit. & Parasitic Dis.* Moscow. 1945, v. 14, No. 3, 82–6. [In Russian.]

It is well known that cutaneous leishmaniasis usually conveys a lasting immunity, though cases of reinfection are also known ; thus among 1,894 case-histories in Ashkhabad the author found 86 (4·5 per cent.) records of repeated infections. Cases of reinfection are especially liable to occur on transfer from one endemic area to another. In 1940 the author established the presence in Middle Asia of two types of oriental sore, the " dry", urban form, and the " moist", rural form [see this *Bulletin*, 1944, v. 41, 331]. On analysing the above 86 cases of reinfection, it was found that 18 patients originally had the first form, later acquiring the second form, while in four cases the sequence was reversed ; whereas in 62 patients the type of the original infection remained unknown. Moreover, in some cases the two types of sores developed independently in the same subject. It was suggested that there was no cross-immunity between the two types of cutaneous leishmaniasis.

The author records further observations confirming this view. In 1942 a large group of schoolchildren from Ashkhabad, where the " dry " variety of oriental sore is prevalent, spent one to two months on field works in an endemic area of the " moist " variety, with the result that 59 per cent. of the children acquired an infection with the latter type of the disease. It was ascertained that of 300 children, 49 had formerly suffered from the " dry " form of the disease, 10 had been vaccinated with this variety, while two had previously had sores of the " moist " type. In 44 children there was circumstantial evidence of previous infection with the " dry " form, whereas in 45 no data were available. In 55 per cent. of the cases a previous infection with oriental sore of the " dry " type failed to protect against infection with sores of the " moist " type. However, a previous infection with the former type reduced the severity of the second infection, pointing to some degree of group immunity. Further confirmation of the strain-specificity of the immunity was provided by the results of vaccination : inoculation of cultures of leishmania isolated from sores of one type protected against infection with the homologous sores, but not against heterologous sores. Finally, there is evidence that, in rare cases, there may be reinfection after five to nine years, with sores of the same type as in the primary infection.

It is concluded that cross-immunity between the two types of oriental sore is absent or only slightly developed, and that the course of infection with a heterologous type is milder than in the primary disease. In prophylactic vaccination against cutaneous leishmaniasis, either the strain used should correspond to the type of sore prevalent in the locality, where the vaccinated person proposes to reside, or strains of both types should be used.

C. A. Hoare.

FILATOV, V. P. **Tissue Therapy in Cutaneous Leishmaniasis.** *Amer. Rev. Soviet Med.* 1945, Aug., v. 2, No. 6, 484–90, 14 figs. on 2 pls.

Under the term " tissue therapy " the author describes a procedure which he states is based on a new principle in medicine. He holds that animal and plant tissues, when preserved under adverse conditions, generate biogenic substances which stimulate healing and regeneration when they are introduced into the body. The introduction may be made by various methods—grafting, implantation, subcutaneous and intramuscular injection, surface applications, rectal injections. The author claims that a great many diseases have been successfully treated by this method ; among these cutaneous leishmaniasis is

specially mentioned in this paper. This has been treated by grafting on to areas from which a piece of healthy skin has been removed a similar piece of skin which had been removed from a cadaver and had been preserved under refrigeration for a week. Within a few days of the skin graftings, which are made at points distant from the sores, changes occur in the leishmania ulcers and healing takes place in two to three months with a minimum of scarring. Similar results were obtained by grafting the preserved skin of the rabbit or by the injection of extract of the leaves of the aloe which had been preserved in the dark. The author concludes that the cases described in the paper demonstrate the powerful effect which tissue therapy exerts in cutaneous leishmaniasis. Grafting of conserved skin and subcutaneous injection of an extract of preserved aloe leaves are equally effective. Tissue therapy acts by virtue of systemic stimulation, independently of the aetiology of an ulcerative process. Thus, tuberculous ulcers, syphilitic ulcers and leishmania ulcers are equally benefited. The paper is illustrated by a series of photographs showing the results of treatment of leishmania ulcers by the author's method.

C. M. Wenyon.

FEVERS OF THE TYPHUS GROUP.

Roy, B. C. **Typhus Fever : with special reference to its Incidence in India.** *J. Indian Med. Ass.* 1946, Feb., v. 15, No. 5, 135–46, 149, 2 figs. (1 map). [89 refs.]

In this clinical description the author uses the name typhus fever as synonymous with the term " fevers of the typhus group", and he seems to favour the unconventional view that all the fevers of the group in India are louse-borne. He states, for example, that " it has not been proved, of course, that Indian typhus is louse-borne, but there is no reason to suppose the contrary. Blood of various arthropod vectors was examined but no definite clue could be obtained."

The paper contains a good deal of useful information, including a table showing the localities in India from which cases have been reported up to 1943, also the vector suggested in each group of cases and the serological type, when this has been recorded. There is a bibliography, which gives references to most of the articles dealing with typhus-group fevers in India, up to 1943 ; but no reference is made to the important observations published since that date.

John W. D. Megaw.

Plotz, H., Wertman, K. & Bennett, B. L. **Identification of Rickettsial Agents isolated in Guinea Pigs by means of Specific Complement Fixation.** *Proc. Soc. Exper. Biol. & Med.* 1946, Jan., v. 61, No. 1, 76–81.

The experiments described in this paper show that the complement-fixation test, as applied by the authors, is the most reliable method of differentiating the rickettsiae of murine typhus, epidemic typhus, and Rocky Mountain spotted fever in guineapigs. The special proviso is that the antigens employed must be purified by washing to remove the " common " antigen.

The results of the experiments are shown in three tables, from which the following analysis has been prepared to show the trend of the responses observed in three lots of guineapigs, each of which received intraperitoneal injections of equal doses of one of the strains of rickettsiae. The data refer to the animals that survived all causes of death long enough to allow the fixation test to be carried out about four weeks after inoculation.

Strain of Infection	Incubation (days)	Fever (days)	Scrotal Reaction		Complement-fixation titre		
			Present	Absent	Epidemic	Murine	R.M.S.F.
Murine (Wilmington) ...	3–7	0–7	31	11	0–80	80–640	0
Epidemic (Breinl) ...	5–19	0–10	4	35	80–640	0–40	0
R.M. spotted fever (mild strain)	2–6	2–9	No mention		0	0	320–640

Some cross-fixation occurred in many of the guineapigs inoculated with epidemic and murine strains, but in every case the titre with the homologous antigen was at least four times as high as with the heterologous. There was no cross-fixation between Rocky Mountain spotted fever and the other two infections.

Two of the 42 guineapigs inoculated with murine rickettsiae had no febrile reaction, but their sera yielded homologous fixation titres of 1–160 and 1–320, and immunity tests showed that they had reacted with inapparent infections.

Six of the 39 guineapigs infected with epidemic rickettsiae had no febrile reaction ; one of these had a fixation titre of 1–160 and was proved to be immune ; the other five remained negative to the test and were non-immune, so they must have escaped infection.

The consistent reliability of the complement-fixation test in the differential diagnosis of the type of infection in inoculated guineapigs is in striking contrast with the uncertain indications yielded by the febrile and scrotal reactions.

[Further investigation will be needed to show whether all strains of these types of rickettsiae can be expected to give equally consistent responses.]

John W. D. Megaw.

GROUPÉ, V. & DONOVICK, R. **On the Specificity of Epidemic and Murine Typhus.** *Science.* 1946, Mar. 15, 330–31.

The existence of specific differences between epidemic and murine typhus fevers has been shown by the following experiments.

Two groups of young Swiss-white-mice were vaccinated ; one group with epidemic vaccine of the Breinl strain, and the other with murine vaccine of the Wilmington strain. Fourteen days later, half of the mice of each group were challenged by lethal doses of toxins obtained from epidemic rickettsiae, and the other half by corresponding doses of murine toxins. The results, observed 18 hours later, were :—(1) Of 23 mice vaccinated by epidemic vaccine 20 survived the dose of epidemic toxin, whereas all the 23 vaccinated by the same vaccine, and challenged by murine toxin, died. (2) Correspondingly, of 23 mice vaccinated by murine vaccine 22 survived the dose of murine toxin, whereas all the 23 vaccinated by murine vaccine and challenged by epidemic toxin, died.

These findings are opposed to those reported by FITZPATRICK, who obtained results suggesting that the epidemic and murine toxic factors are identical [this *Bulletin*, 1945, v. 42, 793].

John W. D. Megaw.

DICK, J. C. **Notes on the Weil-Felix Reaction in Typhus Fever and other Diseases.** *J. Path. & Bact.* 1946, Jan., v. 58, No. 1, 21–30. [24 refs.]

Between March 1942 and February 1944, 505 Weil-Felix tests were carried out on 308 cases of various fevers, including 80 of typhus, in a hospital in the

Middle East. Standard R.A.M.C. suspensions and Dreyer's tubes were used. The results were read after overnight incubation at 37°C. The end point was "the last tube in which a definite ring of particles could be obtained by rotation, and seen by the naked eye at the neck of the tube" with examination in a strong light against a dark background. In these conditions, within the first 10 days of illness a titre of 1–240 was regarded as "slightly suggestive" of typhus, and one of 1–480 as "very suggestive". At any stage, a titre over 1–480 was considered as "definitely positive".

At first all the three usual strains of *Proteus* were used, but it was soon found that non-specific reactions with *OXK* were relatively common at titres of 1–480, and even titres of 1–960 with this strain could not be regarded as definitely positive, so that in the absence of evidence of the existence of mite-borne typhus in the area the *OXK* test was discarded.

In 68 of the 80 cases of typhus fever, rickettsia-agglutination tests were carried out by VAN ROOYEN, who diagnosed 21 of them as epidemic (louse-borne), 36 murine (flea-borne), and 11 as incapable of being differentiated by the test.

Among the 80 cases of typhus the Weil-Felix titre (*OX19* or *OX2* or both) rose to above 1–480 in 73, and to 1–480 in the remaining seven. The earliest "definitely positive" reaction occurred on the 6th day, and in observations made after the 10th day the titre fell below 1–480 in only two cases, both of which yielded titres above 1–480 at a later date.

The titre with *OX19* was usually higher than that with *OX2*, but in six murine cases, and one other, the positive titre was reached with *OX2* and not with *OX19*.

No evidence, clinical or bacteriological, could be found "to warrant the claim that the cases of *OX2* agglutination studied were due to tick-borne infection." [The possibility that tick typhus might occur in "M.E.F. and Egypt" was suggested by the reviewer, who stated that it would be surprising if the tick-borne disease were absent from the area, which included Egypt, Palestine, and parts of Iraq and Persia (this *Bulletin*, 1945, v. 42, 195)].

Among 26 cases of typhoid fever titres of 1–120 or over were observed in nine patients, and in three of these the titre with *OX2* reached 1–240. Among 28 cases of paratyphoid A or B, a titre of 1–240 was reached in eight. In one patient with paratyphoid B, a double infection was considered possible because the titre with *OX19* and *OX2* was 1–960 on the 14th and 16th days, and by the 90th day the *OX19* titre was 1–60 and the *OX2* titre was 1–30; all the other evidence, however, was opposed to the existence of typhus infection in this case. In two cases of paratyphoid A, titres of 1–240 with *OX19* and 1–120 with *OX2* were observed on the 5th and 8th days respectively, but by the 27th and 32nd days the titres had fallen to 1–30. Rising-titre agglutinations at low levels occurred with *OX2* in typhoid, and with *OX19* and *OX2* in paratyphoid in some cases, so the author advises that care should be exercised in the interpretation of such reactions.

In 166 cases of fevers other than typhus and the enteric group, 268 Weil-Felix tests were carried out at various stages. In 22 cases no agglutination occurred; in 80 the maximum titres with *OX19* or *OX2*, or both, were 1–30 or 1–60; in 52 the maximum titre was 1–120; in 10 it was 1–240; and in two it was 1–480. Titres of 1–60 or under are regarded as insignificant. In most of the non-specific agglutinations with titres of 1–120 or over the highest titre was usually observed early and a fall soon occurred, but sometimes the titre remained fairly constant, and in a few cases a rising titre was observed. Non-specific agglutination was more frequent with *OX2* than with *OX19*.

Among six cases of measles, three reacted at 1–120 with *OX2*, and a fourth had a titre of 1–480 up to the 7th day, after which the titre fell. One case of

" common cold " gave a titre of 1–480 (*OX2*), and two of influenzal broncho-pneumonia reached 1–240 (*OX2*). In two of eight cases of infective hepatitis a titre of 1–120 (*OX19* and *OX2*) was observed in the later stages. In several cases of "pyrexia of unknown origin" repeated tests were made ; the titre never arose above 1–250. In a case of lymphadenoma the findings were confusing as can be seen from the table below :—

Day of disease	Agglutination titres				
	OX19	*OX2*	*OXK*	Epidemic rickettsiae	Endemic rickettsiae
13	0	0	480	0	500
27	60	240	960	0	500
64	60	120	480	0	200

In a case of tonsillitis with an irregular rash, in which diphtheria occurred as a complication on the 16th day, the titres with *OX19* and *OX2* were :— 6th day, 1–30 ; 14th day, 1–120 ; and 23rd day, 1–240. In a case of dysentery with indefinite exudate the *OX19* titre was 0 on the 3rd day and 1–120 on the 8th day.

Attacks of murine typhus occurred in two persons who had been inoculated against typhus six and eight weeks previously ; in both, the Weil-Felix reaction developed in the usual way. So also, in five inoculated persons who suffered from fevers other than typhus, the agglutination responses did not differ from those occurring among uninoculated persons in otherwise similar conditions.

The author suggests that the non-specific reactions may have been due to previous inoculation with T.A.B. vaccine and tetanus toxoid, which had been received by all the patients in the series, and which " appear to have had some effect in activating the patient's 'shadow factories' for manufacturing agglutinins." The great majority of the patients were British, and none of the others had come from places where typhus fever was endemic.

John W. D. Megaw.

ANDREWES, C. H., KING, H. & WALKER, J. **Chemotherapeutic Action of Dyes in Typhus Infection of Mice.** *Brit. J. Pharmacol.* 1946, Mar., v. 1, No. 1, 15–20.

This important paper is published in the first number of the *British Journal of Pharmacology and Chemotherapy*, which makes a welcome, though belated, appearance. Some points of general interest are as follows :—Among the substances already found therapeutically active in typhus infection of mice are methylene blue, toluidine blue, and other dyes of the thiazine group. The authors, with VAN DEN ENDE, had already carried out routine tests of methylene blue and toluidine blue on infected mice, but had failed to find any benefit, presumably because the drugs were badly tolerated when administered by the peritoneal route employed in the experiments. These and some other dyes have now been tested on mice infected by the nasal route according to the technique already described by the authors [this *Bulletin*, 1945, v. 42, 20]. Various doses of methylene blue and toluidine blue were administered to the mice : (1) mixed with their food ; (2) by the oesophageal route, using measured doses ; and (3) subcutaneously. Both dyes in suitable doses completely suppressed the development of lung lesions when administered by any of these methods. A murine strain of rickettsia was used, but in two tests of toluidine blue, epidemic rickettsiae were employed, and the results were rather less satisfactory.

A large number of dyes were tested for *in vitro* activity by mixing suspensions of murine rickettsiae with solutions of the dyes, keeping the mixtures at room temperature for 45 minutes, and then injecting them intradermally into the shaved skin of rabbits. It was found that methylene blue, toluidine blue, six other dyes of the thiazine group, and selenium methylene blue, in dilutions of 1–500,000, prevented the development of the Giroud reaction. Various acridine dyes, including proflavine, acriflavine, and atebrin, were ineffective in strengths of 1–2,000. The results of this test do not always agree with those obtained with the mouse test; for example the drugs "V 147" and "V 186," which had already been found by the authors to be more effective than methylene blue or toluidine blue in the treatment of mice, showed no activity when subjected to the rabbit intradermal test.

PETERSON had already shown that toluidine blue inactivated murine rickettsiae *in vitro* and also had a therapeutic action when administered to infected mice with their food [this *Bulletin*, 1944, v. 41, 935].

Mention is made of the successful treatment of typhus-infected mice with methylene blue by KIKUTH and SCHILLING [*Zent. f. Bakt.*, 1. Abt., Orig., 1944, v. 151, 293]. *John W. D. Megaw.*

SACHS, A. **Typhus Fever in Iran and Iraq, 1942–43. A Report on 2,859 Cases.** *J. Roy. Army Med. Corps.* 1946, Jan. & Mar., v. 86, Nos. 1 & 3, 1–11; 87–108, 14 figs. on 3 pls., 2 graphs & 7 charts. [17 refs.]

[This report will supply valuable material for the typhus-fever chapter of the medical history of the recent war. In the present abstract it is possible to deal with only a few of the interesting observations recorded by the author.]

The disease among British and Indian troops in the area during 1942–43 conformed closely in most respects to the pattern seen in the Mesopotamia campaign during 1917–18; even the case-fatality rate (21·9 per cent.) was much the same as in the previous war, when it was 22·75 per cent.

Considering the degree of exposure to infection, the incidence among the troops was low—0·78 per mille during the first seven months of 1943. Disinfestation with the powder "A.L. 63", containing derris and naphthalene, was regarded as giving satisfactory results. A Cox-type vaccine was available for about one-fourth of the troops, including some exposed to special risk. Among the vaccinated subjects the incidence was 0·37 per mille; among the unprotected it was 0·91 per mille. Only two deaths occurred among the 51,000 protected, against 33 among 155,000 unprotected. No attacks occurred later than six weeks after the third dose of vaccine had been given.

Sulphapyridine was given to 336 patients, but even when the administration was started before the fifth day there was no reduction in the incidence of bronchopneumonia or in the fatality rate.

The clinical features of the disease were similar to those usually noted in outbreaks of a corresponding kind, but a curious observation was that in 55 per cent. of the fatal cases in North Iran, death was attributed to circulatory failure or pulmonary oedema, whereas in South Iraq these conditions were not reported as having occurred in any case. In one group of 60 cases, acute abdominal symptoms occurred in three patients, one of whom recovered after an exploratory operation; the other two died, one of them two weeks after an operation for appendicitis, and the other without surgical intervention. In these two fatal cases, haemorrhages into the wall of the caecum, and massive sub-pericardial haemorrhage, were found after death.

The morbid histology of the disease was closely studied, and the characteristic vascular lesions were found; but, in addition to the usual "typhus nodules" associated with the small vessels of the brain, there were also nodules in the

brain which had no apparent connexion with the vascular system. The detailed description of the microscopic changes is illustrated by 14 good photomicrographs, and in three of these rickettsiae are shown. For the demonstration of rickettsiae, a slight modification of Wolbach's technique was employed :—after fixation of the tissues for 24 hours in Zenker's fluid, paraffin sections were cut and treated with xylol, ether, and various dilutions of alcohol. The sections were stained for 12–18 hours in a mixture consisting of :—distilled water, 100 cc. ; 0·5 per cent. sodium bicarbonate solution, 2–4 drops ; methyl alcohol, 3 cc. ; and Giemsa's stain, 2·5 cc. Differentiation was by acetone.

A Weil-Felix titre, with *Proteus OX19*, rising rapidly to 1–100 or more, was regarded as suggestive. The percentage of sera in which titres of 1–1,000 or over were reached in the second week was about 30 among British and Indian troops, but only about 9 among Iranian civilian patients ; in the fourth week the figures were even more strikingly different, 50 per cent. and 8 per cent., respectively. On the other hand, titres of 1–100 or over were reached by the 5th to the 7th day in 50 per cent. of the civilian patients and in only 24 per cent. of the military cases.

Proteus OX2 was agglutinated at titres equal to, or higher than, those obtained with *OX19* in 10 per cent. of the sera from Iranian patients examined.

In a series of 81 sera of typhus patients from the area, VAN ROOYEN found that the rickettsia-agglutination reaction was of the epidemic type in 75, and of the murine type in 6.

A " Precipitin Colloid Test (Platinum Chloride)", devised by Major L. E. ELKERTON, I.M.S., was tried. The antigen used was a mixture of four volumes of supernatant fluid taken from a rickettsia vaccine after standing for " some time " and three volumes of a 0·664 per cent. solution of platinum chloride. To 18 drops of distilled water (pH 6·6) one drop of serum is added ; after shaking, one drop of antigen is added, the mixture is shaken and 18 more drops of distilled water are added. Readings of the turbidity are then made. Positive reactions are said to occur earlier than with the Weil-Felix test, and are regarded as indicating the presence of antibodies of the specific infecting agent rather than the *Proteus* agglutinins.

Numerous guineapigs were inoculated intraperitoneally with the blood of patients. With the usual suspensions of macerated blood clot, typhus was transmitted from 8 of 31 cases, but better results were obtained by centrifuging 20 ml. of blood mixed with 4 ml. of sterile citrate solution, and using 2 ml. of the leucocyte and upper red-cell layer thus obtained as the inoculum. With this method, five positive results were obtained in ten cases. Blood drawn in the first week gave the best results ; samples taken in the second week were slightly less suitable, and third-week samples were seldom positive.

The febrile reaction in guineapigs was better shown when the intra-abdominal temperature was taken instead of the rectal temperature.

The morbid anatomy of the infected guineapigs is described in detail. VAN ROOYEN, who examined 31 of the infected guineapigs, found that the Iran-Iraq strains of epidemic typhus rickettsiae differed from the Egyptian in being more virulent, causing (1) a tunica reaction (though this did not amount to a true scrotal reaction) ; (2) petechial haemorrhages into the peritoneum ; and (3) in many cases, nodule formation in the brain such as was never seen among 200 guineapigs infected with the Egyptian strains. *John W. D. Megaw.*

VIOLLE, H. & CALAMET, L. Sur une épidémie de typhus survenue à Marseille au camp d'hospitalisation des prisonniers allemands. [**An Epidemic of Typhus in a Hospital Camp for German Prisoners in Marseilles.**] *Bull. Acad. Méd.* 1946, v. 130, Nos. 12, 13 & 14, 229–31.

LEVADITI, J. C. & PANTHIER, R. La microscopie en fluorescence de *Rickettsia prowazeki*. [**Fluorescence Microscopy of** *Rickettsia prowazeki*.] *C. R. Soc. Biol.* 1945, Oct., v. 139, Nos. 19/20, 890–92. [Refs. in footnotes.]

Rickettsia prowazeki, obtained from the lungs of infected rabbits, were examined microscopically by ultra-violet illumination. They were found to possess no natural fluorescence and although they could be made visible by staining with electro-positive fluorescent dyes they appeared identical in size and form with the organisms stained by ordinary dyes and examined with white light. Fluorescence microscopy, therefore, does not reveal any structural details such as have been observed with the electron microscope.

John W. D. Megaw.

LEÓN, A. P. Reacción de Weil-Félix tipo Kahn. [**The Kahn-Type of Weil-Felix Reaction.**] *Rev. Inst. Salubridad y Enfermedades Trop.* Mexico. 1945, Sept., v. 6, No. 3, 173–9. English summary.

The test described appears to be a rapid modification of the Weil-Felix test. The apparatus employed is the same as that used in the Kahn test for syphilis, and the procedure is on similar lines except that the antigen consists of a highly concentrated and standardized suspension of *Proteus OX19*, and that 0·1 cc. of the serum to be tested is used instead of 0·15 cc.

The reading is made within 10 minutes ; the tubes are kept in the rack, and neither a lens nor a concave mirror is used.

The degree of agglutination in each of the three tubes is recorded as +; ++ ; +++ ; and ++++. When a total of 8–12 crosses is recorded in the three tubes the reaction is regarded as " positive", when the total is 2–7 crosses it is " doubtful", and with less than two crosses it is " negative".

In a series of 33 tests of typhus sera in which the Weil-Felix titre ranged from 1–160 to 1–10,240, the reaction was positive in 30 ; it was doubtful in three, in each of which the titre was 1–160.

In a group of 18 cases of typhoid fever there were no positive, but 11 doubtful, reactions ; in this group the Weil-Felix titres ranged from 1–20 to 1–160.

Among 828 sera sent for the diagnosis of syphilis, 466 gave doubtful, and 11 gave positive, responses ; among the same sera 628 gave Weil-Felix titres ranging from 1–20 to 1–160, and two gave titres of 1–320 and 1–640 respectively. The 11 sera that gave positive reactions with the author's test reacted at titres of 1–80 to 1–640 with the Weil-Felix test.

John W. D. Megaw.

LEÓN, A. P. & CANO, Carmen. La reacción de "fijación del complemento inversa " en el diagnóstico del tifo exantemático. [**The " Inverse Complement-Fixation Test " in the Diagnosis of Typhus Fever.**] *Rev. Inst. Salubridad y Enfermedades Trop.* Mexico. 1945, Sept., v. 6, No. 3, 167–72. English summary.

The authors have confirmed the findings of SMORODINTZEFF and DROBYSHEVSKAYA, who showed that the presence of a specific antigen could be demonstrated during the first few days in many cases of typhus fever [this *Bulletin*, 1944, v. 41, 1021].

In the present experiments the complement-fixation test was carried out by using known antibodies instead of known antigens. The antibodies were obtained by immunizing rabbits with intravenous injections of *Rickettsia prowazeki* var. *mooseri*, or of *Proteus OX19*.

All of nine typhus patients whose sera were tested before the 10th day of the illness gave strongly positive reactions. The average titre of two of these, tested before the 5th day, was 1–3,000 ; the other seven were tested between the 5th and 10th day, and the average titre was 1–900.

Among 13 patients tested after the 10th day, only four reacted ; the average titre was 1–300. In all of four convalescent typhus patients, and in 13 typhoid patients, the reaction was completely negative.

The reaction, therefore, appears to be specially useful in the early stages of typhus attacks, while the free antigens are still dominant and the standard complement-fixation test, based on the presence of antibodies, is still negative in most cases. *John W. D. Megaw.*

D'IGNAZIO, C. & CODELEONCINI, E. Dermotifo in vaccinati. Nota clinica. [**Typhus Exanthematicus in Vaccinated Persons. A Clinical Note.**] *Boll. Soc. Ital. di Med. e Igiene Trop.* (Sez. Eritrea.) 1945, v. 5, No. 4, 7–21.

Evidence is produced to show that the original Weigl-type vaccine and a locally produced vaccine have had a striking effect in lessening the severity of attacks of typhus fever among European patients in Addis Ababa during the years 1938–41.

There were 55 cases, of which four were fatal, among vaccinated persons. One of the patients who died was attacked before the end of his course of vaccination, and the other three had not been revaccinated during the previous three years. The case-fatality rate among unvaccinated patients was about 21 per cent. *John W. D. Megaw.*

IMBROSCIANO, G. Sul valore teorico e pratico delle intradermoreazioni con i polisaccaridi del *Proteus X19* e della *Rickettsia prowazeki* per la diagnosi di dermotifo. [**The Theoretical and Practical Value of the Intradermal Reaction with the Polysaccharides of *Proteus X19* and of *Rickettsia prowazeki* in the Diagnosis of Exanthematic Typhus Fever.**] *Giorn. di Batteriol. e Immunol.* 1945, Oct.–Dec., v. 33, Nos. 10/12, 193–216. [11 refs.] English summary.

The author has isolated the polysaccharide of *Proteus X19* by the method of ZINNSER and PARKER, and, using CASTAÑEDA's technique, he has obtained from this two fractions—the OX and OP factors. Both fractions, together and separately, were used in carrying out the intradermal tests. Rickettsial polysaccharides were also prepared from the intestines of infected lice by Castañeda's method. All the above substances were used in dilutions of 1–160,000 and 1–640,000. A filtrate of *Proteus* cultures was also employed in dilutions of 1–100 and 1–200.

The responses to intradermal injections of all these preparations were essentially similar :—inflammatory reactions in healthy persons and in patients suffering from diseases other than typhus, also in persons vaccinated with Weigl's vaccine ; negative results in typhus patients from the 5th or 6th day onwards ; and variable responses in typhus convalescents.

The test is regarded as specific and therefore of diagnostic value. A significant response is said to have been obtained in some cases before the Weil-Felix reaction became positive. False positives were observed in some cases when the *Proteus* filtrate was used ; these were regarded as being due to sensitiveness of the patients to non-specific proteins contained in the culture medium.

Details of the methods employed and of the responses obtained in a large number of cases are contained in the paper. *John W. D. Megaw.*

MILLER, E. S. & BEESON, P. B. **Murine Typhus Fever.** *Medicine.* 1946, Feb., v. 25, No. 1, 1–15. [30 refs.]

This description of murine typhus fever is based on a study of 126 cases seen at Atlanta, Georgia, during the eight years ending 1943. The diagnosis was based

on the observation of a clinical picture consistent with typhus fever, together with a positive Weil-Felix reaction at a titre of 1–160 or over. Some cases in which the Weil-Felix reaction was positive were excluded because of the presence of a *Proteus* infection, and there were other cases, including three fatal, in which the clinical picture suggested murine typhus but in which the diagnosis could not be confirmed by a positive Weil-Felix test.

Contrary to the usual belief, the disease was as common among negroes as among white men. The month-by-month incidence, starting from January, was :—3, 2, 0, 0, 2, 3, 11, 19, 32, 30, 17, 7.

There was a definite history of association with rats in 54 per cent. of the cases, but only two patients " could recollect having been bitten by fleas " ; so that the authors doubt whether infection is conveyed solely through actual contact with fleas ; contact with faeces of the insects or with urine of infected rats must be considered as possibilities.

The clinical features are described ; they correspond to those of louse-borne typhus of a mild type. A rash was seen in 90 per cent. of the white and in 43 per cent. of the negro patients. The percentage distribution of the rash was trunk, 98 ; upper limbs, 75 ; lower limbs, 59 ; palms, 14 ; soles, 10 ; and face, 10.

The only patient who died was a negro woman, aged 60, who had uraemia on admission. There may have been three other fatal cases during the period among patients with unconfirmed diagnosis. *John W. D. Megaw.*

PHILIP, C. B., WOODWARD, T. E. & SULLIVAN, R. R. **Tsutsugamushi Disease (Scrub or Mite-borne Typhus) in the Philippine Islands during American Re-Occupation in 1944–45.** *Amer. J. Trop. Med.* 1946, Mar., v. 26, No. 2, 229–42, 1 fig. [11 refs.]

The authors state that " it is remarkable that incontrovertible evidence of tsutsugamushi disease in the Philippine Archipelago was not forthcoming until its occupation, in troops . . . during the present war." They think it likely that cases described by ASHBURN and CRAIG in 1908 [see this *Bulletin*, 1944, v. 41, 437], and other cases reported by FOSTER in 1912, under the name " endemic typhus", may have been instances of tsutsugamushi disease.

The present paper deals with the disease as observed during the reoccupation in 1944–45.

Altogether 222 cases, of which 10 were fatal, have been recorded, from the following islands :—Mindoro, 95 ; Samar, 88 ; Luzon, 28 ; Negros, 7 ; Leyte, 3 ; and Mindanao, 1. An eschar was seen in 40·5 per cent. of the patients, and a rash in 21·2 per cent. These figures are thought to be under-estimates.

Most of the cases in Luzon were closely investigated ; in 15 of them samples of sera were tested by the complement-fixation test by Dr. Ida BENGTSON [whose name, as often happens, is wrongly spelled as " Bengston "]. The reaction was positive in every case ; the titre ranged between 1–64 and 1–32,768 in 14 cases.

The authors isolated a virulent strain of *Rickettsia orientalis* from a patient in Samar Island ; this strain was subjected to stringent tests.

The infected localities were usually grass-covered land, or neglected and scrub-infested coconut groves. *Trombicula deliensis* (syn. *T. walchi*) was found on rats in all the Islands in which the disease occurred except Leyte Island. *T. akamushi* (syn. *T. fletcheri*) was found in Luzon and Negros. The most important of the mite hosts appeared to be *Rattus mindanensis.*

John W. D. Megaw.

IRONS, E. N. **Clinical and Laboratory Variation of Virulence in Scrub Typhus.** *Amer. J. Trop. Med.* 1946, Mar., v. 26, No. 2, 165–74. [11 refs.]

The author states that there is no reliable evidence to show that variations in the virulence of *Rickettsia orientalis* are reflected in the severity and mortality of scrub typhus. He discusses two groups of cases of the disease in the South-West Pacific area ; the clinical data were as shown in the table :—

	Area A	Area D
Number of cases	449	1,255
Percentage mortality	7·1	0·6
Percentage showing eschars	89	51
Average duration of fever in days	18	14·6
Average day of initial Weil-Felix	16	10

In area A, 32 consecutive attempts to isolate rickettsiae yielded 31 positive results from the intraperitoneal injection of triturated blood-clot into white mice. All the strains were equally virulent, killing the mice in 10–18 days. Two of the strains were maintained by serial passages through mice, which died, on the average, 7 days after inoculation.

In area D, strains were isolated in all the eight cases tested, but only four of the strains were lethal to the mice, the other four caused inapparent infection, as shown by the immunity of the animals to 1,000 m.l.d. of a virulent strain. The strains that caused apparent attacks were passaged and caused the death of inoculated mice in the average period of 9–10 days, and when tested on guineapigs and rabbits they showed consistently less virulence than the strains from area A.

[The well known variations in the severity of the disease in different outbreaks had already provided strong *prima facie* evidence of the existence of strains of high and low virulence. The present experiments can be regarded as supplying final proof in the matter.] *John W. D. Megaw.*

HAMILTON, H. L. **Growth of the Rickettsiae of Tsutsugamushi Fever on the Chorioallantoic Membrane of the developing Chick Embryo.** *Amer. J. Path.* 1946, Jan., v. 22, No. 1, 89–101, 13 figs. on 2 pls.

A vascular nodular mass was produced on the chorioallantoic membrane of 10-day embryo chicks by inoculating intraperitoneal exudate from mice infected with *Rickettsia orientalis*. The nodule was usually about 8–10 mm. in diameter and 4–6 mm. in thickness after seven days' growth, and its outer surface was ulcerated. The lesion has been reproduced throughout 26 successive transfers. The first stage in its formation was a proliferation of mesenchyme cells round centres of rickettsial multiplication ; later the cells in the middle of each focus of proliferation became necrosed.

The appearance of the nodule is well illustrated by two photographs, its structure is described in detail and is illustrated by three low-power photomicrographs of sections at different stages of its development.

Similar nodules have been produced by LEWTHWAITE and O'CONNOR (*Rep. Virus Lab., Commonwealth Serum Lab.*, Melbourne, 1943) who, however, did not study them but referred to this method of inoculation as having given " poor results".

The author has found that rickettsiae of Rocky Mountain spotted fever give rise to nodules of the same kind, but without ulceration, and that rickettsiae

of boutonneuse fever cause a greyish thickening of the membrane, but there is no time for the production of a nodule because the embryo dies of infection within three or four days.

ZIA [this *Bulletin*, 1935, v. 32, 162] found that rickettsiae of epidemic and Mexican typhus sometimes gave rise to the formation of small nodules on the membrane, but the usual reaction was a simple thickening at the site of inoculation. *John W. D. Megaw.*

WOLFE, D. M., VANDERSCHEER, J., CLANCY, C. F. & COX, H. R. **A Method for the Preparation of Complement-Fixing Antigens in a Study of Experimental Tsutsugamushi Disease (Scrub Typhus).** *J. Bacteriology.* 1946, Feb., v. 51, No. 2, 247–55.

The authors have worked out a method of large-scale preparation of the complement-fixing antigens from yolk-sac cultures of *Rickettsia orientalis.* The method is said to be applicable also to the preparation of diagnostic antigens for louse-borne typhus, murine typhus, Rocky Mountain spotted fever, and American Q fever. The immunizing properties of the antigens are being tested with a view to their possible employment as a vaccine. Full details of the technique are given in the paper; a general outline is as follows. Large numbers—300 to 900 daily—of fertile hens' eggs were inoculated; the yolk-sac membranes, which were found to be specially rich in rickettsiae, were harvested on the 8th to the 11th day according to the degree of multiplication of the organisms as ascertained by the daily examination of smears from 12 or more eggs. It was usually possible to obtain an average rickettsial growth of "one plus", in which smears showed from six to a countable number of rickettsiae in each microscope field; smears with uncountable numbers were termed "two plus".

The yolk-sac membranes were weighed and homogenized to make a 50 per cent. suspension in phenolized (0·8 per cent.) distilled water. After 48 hours at 4°C. the suspension was frozen and completely dried *in vacuo.* The resultant material was broken up and treated twice with ether for three to four hours at 4°C., with occasional shaking. After complete removal of the ether the remaining dried powder was suspended in phenolized (0·3 per cent.) saline, stored for three to five days at 4°C., with occasional shaking, and centrifuged at 3,000 per minute for 30 minutes. The supernatant fluid constituted the antigen used in the experiments.

The antigens were found moderately active and strictly specific when subjected to complement-fixation tests; sera of guineapigs convalescent from tsutsugamushi disease reacted up to a titre of 1–128, whereas all the sera of guineapigs convalescent from epidemic typhus, endemic typhus, Rocky Mountain spotted fever, and American Q fever gave negative responses at a titre of 1–8 or less. *John W. D. Megaw.*

SHEPARD, C. C. & TOPPING, N. H. **Rocky Mountain Spotted Fever. A Study of Complement Fixation in the Serum of certain Dogs.** *J. Infect. Dis.* 1946, Jan.–Feb., v. 78, No. 1, 63–8.

The circumstances leading up to the initiation of the present study were as follows:—A fortnight after arrival at a resort in Long Island a dog belonging to Mr. B. was attacked by fever which lasted about nine days; 19 days later Mr. B. was attacked by Rocky Mountain spotted fever. Sera from Mr. B. and his dog gave strongly positive reactions with the Weil-Felix (*Proteus OX19*) and the complement-fixation (Rocky Mountain spotted fever antigen) tests.

Sera of 98 dogs from the same and other localities were then examined by the complement-fixation test; titres of 1–256 or over were observed in 11 animals, of which eight belonged to families in which cases of Rocky Mountain spotted fever were said to have occurred. Among 41 of the dogs that lived in localities in which Rocky Mountain fever was not known to occur there was only one positive reaction, at a titre of 1–128, and no other at a titre above 1–16. For technical reasons the reaction at 1–128 was not regarded as being significant.

Some of the human patients gave no history of having been bitten by ticks, but were known to have picked ticks from their dogs.

The authors state that the findings suggest more than a casual association between the dog and human cases, but that further studies will be needed to elucidate the rôle of the dog in the epidemiology of the disease. They also point out that the dog has been implicated as the reservoir of the tick-borne boutonneuse fever, and that Rocky Mountain fever has been transmitted experimentally to dogs by the bites of infected ticks [this *Bulletin*, 1933, v. 30, 896]. *John W. D. Megaw.*

YELLOW FEVER.

GARNHAM, P. C. C., HARPER, J. O. & HIGHTON, R. B. **The Mosquitos of the Kaimosi Forest, Kenya Colony, with special reference to Yellow Fever.** *Bull. Entom. Res.* 1946, Feb., v. 36, Pt. 4, 473–96, 3 text figs. & 6 figs. on 2 pls. [21 refs.]

Two cases of yellow fever have occurred in Kenya in recent years, one at Kitale (1942) and the other at Kisumu (1943). To ascertain if Kenya forests are infected or if conditions in them are suitable for the development of the disease, investigations were started in November 1942, and continued until October 1944.

The Kaimosi forest lies north of the equator between Kisumu and Kitale. It is a semitropical rain forest covering some 50 square miles; the locality, vegetation, inhabitants and climate are first described and then a more detailed account is given of the mosquitoes of the area.

Adult mosquitoes were collected at ground level and on a fixed platform 55 ft. up a tree in the depth of the forest; they were also taken on a movable platform at different levels. Animal-baited traps attracted nothing, and collecting in huts yielded only small numbers. Larvae were taken at different heights from rot-holes in trees; from axils of plants; from bamboo and wooden containers slung in trees; from bamboo sections placed on the fixed platform in the tree top and from many other places. The authors propose the term "acrodendrophily" to indicate the preference shown by certain mosquitoes for haunting tree tops.

The routine collections produced 55 species of ten genera, of which the following are some examples. *Culex nebulosus* was found at most levels even as high as 60 ft. The commonest larva in tree holes was that of *Aëdes capensis*, though adults were rare. *Aëdes apicoargenteus* was the commonest adult; it bites man readily and prefers light forest; larvae were not found in the routine collecting area, but were taken from holes in fallen trees in the northern part of the forest. In the denser, untouched forest *Aëdes fraseri* larvae were found at all levels, adults occurring in ground and tree top catches in the ratio of 3 : 5. Larvae of *Aëdes longipalpis* were usually absent from ground-level collections, they and the adults were commoner in the tree-tops. *Aëdes aegypti*, a low-level breeder, was never taken in huts, but was frequently found

a mile or more inside the forest, away from human dwellings. *Aëdes africanus*, a known vector of yellow fever, was commonest from August to November; it was found breeding in the buttress roots of trees and in containers up 50 ft. from the ground; adults were taken mostly in the tree tops.

It seems that the selection of a breeding place depends more on height, shade, shape and size than on the chemical composition of the water in it. Analysis of such waters showed that a breeding place of *Theobaldia fraseri* contained 79 parts of oxidizable matter per 100,000 [in Table VI a confusing misprint shows this mosquito as "*A. fraseri*"].

From the evidence accumulated during this survey it is concluded that conditions in the Kaimosi forest are adequate for the establishment of yellow fever; some control measures are suggested. *H. S. Leeson.*

DENGUE AND ALLIED FEVERS.

WEYRAUCH, H. M. & GASS, H. **Urogenital Complications of Dengue Fever.** *J. Urology.* 1946, Jan., v. 55, No. 1, 90–93.

Among 141 U.S.A. males who suffered from dengue in the South-Pacific area in 1943–44, five had "dengue orchitis" as a complication or sequela of the disease. In one case the right testis became swollen and painful in the second month of convalescence, and atrophy was observed six months after the attack. In the other cases orchitis occurred during the febrile stage. In one case the orchitis was unilateral and there was no atrophy; in the other three the condition was bilateral, it was followed in one case by bilateral atrophy, in another by unilateral atrophy, and in the third there was no atrophy.

Five patients, including two who had orchitis, had bloody seminal emissions for one to four months after defervescence. The source of the haemorrhage could not be ascertained. *John W. D. Megaw.*

FLORIO, L., HAMMON, W. McD., LAURENT, Angela & STEWART, Mabel O. **Colorado Tick Fever and Dengue. An Experimental Immunological and Clinical Comparison.** *J. Exper. Med.* 1946, Apr. 1, v. 83, No. 4, 295–301, 4 figs.

Six neuro-syphilitic patients were inoculated with strains of dengue virus obtained from the Pacific area, and in each case a typical attack of the disease was produced; two of the patients were later re-inoculated with the virus, and both were found to be immune. The other four were inoculated 40–80 days later, with a strain of virus of Colorado tick fever which had been serially passaged six times through hamsters and then through two human volunteers. Typical attacks of Colorado tick fever were produced in three of the patients, the fourth had no definite reaction, but he was known to have spent several years in areas where the disease is endemic.

Another patient was inoculated, first with the virus of Colorado tick fever, and 69 days later with the virus of dengue; typical attacks of each disease resulted.

It appeared, therefore, that there was no cross immunity between the two diseases in spite of their striking clinical and haematological similarity and the approximate equality in the particle-size of their causative viruses.

The other chief difference between the diseases are stated to be the absence of rash in Colorado tick fever, the non-transmissibility of dengue through hamsters, and the natural transmission of the diseases by different vectors.

[Colorado tick fever appears to be primarily a disease of lower animals, transmitted from them to man by a tick ; if, as seems possible, it should come to be regarded as belonging to the same disease group as dengue it would be classed as a tick-borne, zootic, member of the group.

The charts illustrating the paper show that there is a remarkable resemblance between the fever curves and haematological findings of dengue and Colorado tick fever. The average duration of the latter fever is slightly longer ; the rise and fall of the temperature are somewhat less abrupt, and no macular or maculo-papular rash occurs. A diffuse erythema was observed in all the dengue patients, but in two only of the four tick-fever patients.

References to earlier work on Colorado tick fever will be found in this *Bulletin*, 1941, v. 38, 694, and 1945, v. 42, 117 and 118.]

John W. D. Megaw.

POLLARD, M., LIVESAY, H. R., WILSON, D. J. & WOODLAND, J. C. **Experimental Studies with Bullis Fever.** *Amer. J. Trop. Med.* 1946, Mar., v. 26, No. 2, 175–87, 7 charts. [11 refs.]

Two of the authors, LIVESAY and POLLARD, have already produced evidence which they regarded as pointing to the probability that the disease was caused by a rickettsia [see this *Bulletin*, 1944, v. 41, 209], and soon afterwards ANIGSTEIN and BADER reported the isolation of an organism which they believed to be a rickettsia [*ibid.*, 666].

After the investigation described in the present paper the authors conclude that " it would be premature to make any definitive classification of the agent without additional studies," and that the agent " appears to approximate in size the elementary body agents such as ornithosis more than it does the typical rickettsiae."

In four cases, the infection was transmitted to human volunteers by subcutaneous injection of serum or blood of infected persons ; in one of these cases the serum of a naturally-infected patient was used after passage through a Seitz E.K. filter pad, but the pad was not afterwards tested for accuracy ; serum from this experimentally-infected volunteer was found infective to another volunteer after passage through a Seitz E.K. pad, which apparently was tested and found accurate. In the other two cases whole blood of naturally-infected patients was employed.

After two preliminary passages through white mice, a strain was passaged serially through the yolk sacs of 5 or 6-day-old chick embryos, and small coccobacillary bodies were found in smears of the sacs, but not inside the cells. [In the previous report of Livesay and Pollard similar bodies were described as occurring inside the cells in peritoneal scrapings from infected guineapigs, and in biopsy smears from lymph nodes of patients.] With yolk-sac material of the 6th to the 20th passage, four volunteers were successfully inoculated.

Three experimentally-infected volunteers were later challenged with blood of patients suffering from Colorado tick fever, and all responded with typical attacks ; so also did a person convalescent from naturally-acquired Bullis fever, when challenged with a hamster strain of Colorado tick fever. It was concluded that there was no immunological relationship between the two diseases.

A strain of infection was obtained from a pooled suspension of the bodies of 337 *Amblyomma americanum* ticks collected from a deer in the area : this strain, after passage through mice and embryo chicks, infected two volunteers who were later found immune to a strain of human origin.

The febrile responses in the experimental cases in human beings were usually slight : in four of the temperature charts two or three fleeting rises to about

99°F. are shown. In all the cases there were relative leucopenia, headache, body aches, and lymphadenopathy.

[The authors refer to the reviewer's suggestion that Bullis fever might be related to Colorado tick fever (see this *Bulletin*, 1944, v. 41, 34, and 1945, v. 42, 375) and although the present observations go to show that there is no immunological relationship between the two diseases, they tend to support the speculative view that both fevers may be caused by filter-passing viruses, related to the virus of dengue. Final judgment on the exact nature of the infecting agent of this elusive disease must be suspended.]

John W. D. Megaw.

LAIGRET, J. & CORCOS, A. Observation à Tunis d'une maladie épidémique se manifestant par de la fièvre et des vomissements de sang. [**Observations on an Epidemic Febrile Disease with Haematemesis, in Tunis.**] *Bull. Acad. Méd.* 1946, v. 130, Nos. 3, 4 & 5, 55–7.

Between mid-September and Mid-November, 1945, the authors saw eight cases of a short, acute, fever, lasting three to five days and ending with haematemesis. Other cases have been seen by their fellow practitioners in Tunis.

The onset and early stages of the illness conformed to the clinical pattern often seen in dengue and sandfly fever, except that a feeling of painful heaviness in the epigastric region, and nausea, were the most prominent symptoms. About the third day the patients suddenly vomited considerable quantities—up to 300 cc.—of red or black blood. Immediate relief followed and the temperature began to fall, reaching normal within about two days. There were two deaths, one in the case of a child aged two years. Although *Aëdes aegypti* were abundant it was possible to exclude yellow fever because of the immediate relief following the haematemesis. Bacteriological investigations yielded negative results. The disease was regarded as a severe form of the " pseudo dengue " which had been prevalent in Tunis since the spring of the same year. There had been hundreds of cases of this fever, which differed from dengue in the complete absence of a rash. Sandfly fever also was ruled out because " neither relapses nor recurrences of the fever were observed." It was concluded that the fever was " like dengue or three-days fever, but was neither the one nor the other," and that a suitable name would be " Tunisian gastroenterrhagic fever."

[The line of reasoning of the authors is not easy to follow. They regard the fever as a severe form of " pseudo-dengue", yet they suggest a name that is obviously unsuitable for a disease of that type. Their only stated reason for excluding sandfly fever—the absence of relapses—is surprising. Altogether the evidence supplied seems compatible with the view that haematemesis may have occurred as an exceptional complication in eight out of several hundred cases of a fever of the dengue group.] *John W. D. Megaw.*

PLAGUE.

BULL. U.S. ARMY MED. DEPT. 1945, Apr., No. 87, 13–16. **Plague in Dakar.**

An outbreak of 567 cases of plague occurred in Dakar, " the largest city in French West Africa," in 1944 during the period April to November, with a 91 per cent. mortality. No cases of plague had been recorded there since 1937, and so this was essentially a war-time epidemic. Most of the interest of this account centres upon the dusting technique and control of the native population. All the actual cases of plague were " in native blacks except one in a Syrian and

three in French Europeans." American help was enlisted for the anti-plague dusting programme, although this was vigorously entered on only after "the seasonal decline of the plague incidence had begun." A division of the native section of the town was made into zones controllable by a cordon of 200 to 300 gendarmes. Each zone was selected the night before operational treatment to prevent exodus, and four or five "outlet stations" were established. Dusting was commenced at about 6 a.m. and was carried out by three or four native workers using 10 per cent. DDT dust, with Hudson plunger-type dusters. The treatment began "at the ankles, dusting under the various layers of clothing, then dusting at the waist—front and rear, then at the sleeves and neck and finally the hair. The clothing was held out and down to form an 'envelope' for the dust which could be seen through the fabric as it was applied on the inside." The operation, to allow of release of the outgoing working native population, was complete in about an hour and then the cordon arrangements were modified to deal with the remaining population. It is reckoned that "less than 5 per cent. of the people were not dusted." Further anti-flea measures consisted in treatment of the houses "by dusting with 10 per cent. dust and by spraying with 5 per cent. solution in kerosene" where attention was specially directed to the floor and lower walls and beds, which were heavily infested with bed bugs as well as fleas. "All public houses such as cafes, restaurants, bars, brothels, cinemas, etc., were sprayed with 5 per cent. DDT solution." A survey showed that of 316 houses infested before spraying "all but 7 were completely free of fleas two weeks after treatment. The rat population in this area was very large, and comprised, more or less equally, the Norwegian, Alexandrian and the common rat. The Camtchouli rat was not so numerous. Poisoning of the rats was barred because of danger to children and domestic animals. French opinion was that the best results in plague treatment was obtained by combined sulphadiazine bacteriophage therapy.

W. F. Harvey.

KARTMAN, L. **A Note on the Problem of Plague in Dakar, Senegal, French West Africa.** *J. Parasitology.* 1946, Feb., v. 32, No. 1, 30–35, 2 figs.

Dakar experienced an epidemic of plague in 1944 and is regarded as an endemic focus. The present communication insists on the possibility of a human flea being a main plague vector in some regions—in Dakar, for example, where the rat flea *X. cheopis*, although the commonest species on rats, is "quite negligible in native huts of the villages about Dakar." Identification of the various species of fleas collected was carried out at the British Museum, and showed that the "house and body" flea in the Dakar area was *Synosternus pallidus*. The genus *Synosternus* is closely related to *Xenopsylla* and the species *S. pallidus* is parasitic on rodents, the hedgehog and various carnivora. A very instructive table gives percentages of various fleas collected for examination :—

Species	From rodents	From floors
	Per cent.	Per cent.
Xenopsylla cheopis	75·95	1·10
Echidnophaga gallinacea	12·85	18·40
Ctenocephalides felis	4·45	0·35
Synosternus pallidus	6·75	80·15

This shows the complete reversal of percentages for *X. cheopis* and *S. pallidus* according as the collection was made from rodent or from the floors of native huts. "It is suggested that further study of *S. pallidus* as a potential vector of plague in the Dakar area is indicated." *W. F. Harvey.*

LAHNUM, W. H. **Mammals and Plague Distribution in the United States.** *U.S. Nav. Med. Bull.* 1946, May, v. 46, No. 5, 782–5.

This contains a useful list of mammals that have been found to be infected or to possess ectoparasites infected with plague.

HORNIBROOK, J. W. **Streptomycin in Experimental Plague.** *Pub. Health Rep.* Wash. 1946, Apr. 12, v. 61, No. 15, 535–8.

Reports are now appearing which deal with the therapeutic possibilities of streptomycin—from *Actinomyces griseus*—in human diseases, especially those due to Gram-negative bacteria. Its toxicity for animals is low and it is more active than streptothrycin. This condensed article, which is full of detail, gives an account of experiments on plague in mice.

The material used contained approximately 200,000 units per gramme, killed a 14-gm. mouse on intraperitoneal injection of 20 mgm. as 5 per cent. solution, and failed to kill a 15-gm. mouse receiving 10 mgm. In the therapeutic tests "treatment was started 3 and 2 days respectively following inoculation with live organisms." If visible swelling at the site of inoculation did not occur the mouse was regarded as non-infected and, together with those that died, was excluded from the testing trials. "At the end of 14 days from the time of inoculation all surviving animals were killed, autopsied, and the spleens cultured" and those mice dying within the 14 days after inoculation of a dose of living plague up to 6,000 organisms in the groin, were considered to have died of plague. A control series, one with no treatment and one with sulphadiazine in the same dosage as streptomycin "except for the first dose which was 5 mg. rather than 2 mg.," was set up, and this series (Table 5) is summarized. The summary of the entire experiments is as follows:—"Streptomycin is thermostable. It is inhibitory to *P. pestis* in broth in a dilution of approximately 1/160,000. . . . When 2 mg. (400 units) . . . were given before and 2 mg. 24 hours after challenge, 10 mice survived for 14 days a dose of plague organisms which killed 70 percent. of the controls. When treatment (2 mg. per day) was started 2 days following inoculation and continued for 6 days, 9 of 10 mice survived for 14 days. When sulfadiazine was used under the same circumstances 4 of 11 survived; 8 of 9 controls died." (Table 5). *W. F. Harvey.*

CHOLERA.

MARKOWITZ, J. **Experiences with Cholera in a Jungle Camp in Thailand.** *J. Roy. Army Med. Corps.* 1946, Apr., v. 86, No. 4, 150–58, 2 figs.

[This is one of a remarkable series of articles written in this number by two prisoners of war in Japanese hands. Undoubtedly the entire series should be given wide publicity for their pictorial and textual illustration of sheer, devilish, human cruelty, and incidentally as testimony to the self-sacrifice and medical ability of the Royal Army Medical Corps "under what may euphemistically be described as adverse conditions." The tales far exceed in their general interest the information relating to particular diseases.]

Much the same type of restricted epidemic, if not identical, has been summarized below. This epidemic relates to a "community of 7,000 more or less disabled British and Dutch prisoners of war." A final table is a "Diary of Events" and shows that of 134 cases admitted as true cholera, 53 were fatal. One concluding remark may be transcribed:—"Anuria resulting in uraemia was an uncommon cause of death. In brief, a patient could die from cholera either from loss of fluid so that his plasma oozed out through the bowels—a

condition comparable to high intestinal obstruction or to shock displayed in a patient grossly scalded by steam ; or he could die of toxaemia as in any other infectious disease." The actual conclusion to the article stresses certain special points in treatment :—distilled water, if taken fresh from the still, is not pyrogenic and can safely be used. Some advantage is claimed for intravenous infusion with 2 per cent. salt solution over 0·85 per cent. (normal) salt solution. " One litre of distilled water hot off the still is treated with 50 c.c's of 25 p.c. sodium chloride stock solution. The latter need not be fresh."

W. F. Harvey.

DE WARDENER, H. E. **Cholera Epidemic among Prisoners of War in Siam.** *Lancet.* 1946, May 4, 637–40, 1 chart.

The account of this cholera epidemic presents the reader with another shocking tale of Japanese barbarism and cruelty to defenceless prisoners of war. It brings into prominence the notorious instance of the construction of the Siam-Burma railway. Some very interesting facts emerge from the details given of what was to a very large extent an untreated epidemic under the worst possible sanitary conditions. It lasted apparently in acute form for about 5 weeks, and seems to have subsided spontaneously. Total figures of cases at risk were 200 British officers and 1,400 British other ranks ; 173 cholera cases were admitted and the deaths among these " admissions " to so-called hospital numbered 100 (57·8 per cent.). A Dutch camp of 250 sick persons afforded a control series ; in this there was only one case of cholera (with recovery) at the same time and under more or less similar conditions to the British. The immunity of the Dutch was not confined to this area, but was observed " in all the camps on the river." As an explanation of what was a very real difference the suggestion is made that recent vaccination (4 weeks previously) and regularly yearly inoculations protected the Dutch and gave them immunity.

Common complications and sequelae are listed as (1) coma, (2) gangrene, (3) multiple abscesses, (4) severe anorexia leading to quick onset of deficiency disease and (5) residual diarrhoea. These same complications, however, seem themselves to have been to some extent complicated by the originally sick state of the population at risk, with chronic malaria, dysentery, beriberi, hyporiboflavinosis and pellagra. As is common in such epidemics the first cases were not recognized. " Facilities for treatment were totally lacking," and the difficulty was increased by the onset of the monsoon.

W. F. Harvey.

BLASS, Judith. Etude de la consommation du glucose par les vibrions cholériques " non proliférants." [**The Consumption of Glucose by " Non-Proliferating " Cholera Vibrios.**] *Ann. Inst. Pasteur.* 1946, Mar.–Apr., v. 72, Nos. 3/4, 230–40, 4 figs.

A new method of preparing cholera toxin was devised by BERNARD and GALLUT [this *Bulletin*, 1945, v. 42, 34, 807] and the present work is designed to study in detail the utilization of glucose in the process. Experimental work is straightforward to determine: (1) the maximum quantity of glucose consumed by a fixed concentration of vibrios, where the variable is the glucose content of the medium ; (2) the consumption of glucose per unit of time with fixed glucose concentration (5/1,000) ; (3) the consumption of glucose as a function of the medium ; (4) the products of fermentation of glucose by the non-proliferating vibrios in Ramon bouillon. Products of fermentation were lactic acid, succinic acid, formic acid, ethyl alcohol and traces of aldehydes, which are the same as those of vibrios grown in synthetic glucose media. The maximum

quantity of glucose utilized was 4 to 5 gm. per litre whatever the concentration of the vibrios, and consumption was accompanied by a fall of *p*H from 8 to 5·8 which was fatal to the vibrios. Increase of concentration of the vibrios produces a more rapid fall in the *p*H. An important factor which determines the utilization of the glucose is the buffering power of the medium.

W. F. Harvey.

AMOEBIASIS AND INTESTINAL PROTOZOAL INFECTIONS.

LAMY, L. Action du para-aminophénylsulfamide (1162 F) sur le départ des cultures d'entamoebadysenteriae. (Deuxième note). [**The Action of Sulphanilamide on the Starting of Cultures of** *Entamoeba histolytica*.] *Ann. Inst. Pasteur.* 1946, Mar.–Apr., v. 72, Nos. 3/4, 295–7.

In a previous paper [this *Bulletin*, 1946, v. 43, 442] the author showed that the presence of sulphanilamide [1162F] was favourable to the development of *Entamoeba histolytica* in cultures ; in the present paper he records experiments which show that in concentrations of 1 : 1,000, 1 : 500 and 1 : 200 it favours the development of the amoebae from cysts in faeces sown on the medium without any preliminary treatment.

Cultures of active amoebae were obtained by the 4th day in all three concentrations of sulphanilamide, but the amoebae were much fewer in that of 1 : 200 than in that of 1 : 1,000. The first subculture, made after 7 days, was positive, and the original culture still showed living amoebae after 10 days ; the medium was the same as that previously used. The addition of rice starch supplied a nutritive factor to the amoebae and also hinders the growth of *Blastocystis*, which is further hindered by the sulphanilamide, as are also bacteria.

The author also refers to abstracts to this *Bulletin* of papers by CHINN *et al.* [1942, v. 39, 765] and by RODANICHE and KIRSNER [1943, v. 40, 455].

J. F. Corson.

TSUCHIYA, H. & KENAMORE, B. **Report on a Case of Balantidiasis.** *Amer. J. Trop. Med.* 1945, Nov., v. 25, No. 6, 513–14.

The case reported was in a woman 35 years of age who had suffered from persistent diarrhoea associated with abdominal pain of four months' duration. There was no history of contact with pigs. The condition was cured by carbarsone treatment.

C. M. Wenyon.

RELAPSING FEVER AND OTHER SPIROCHAETOSES.

PAVLOVSKY, E. N. [**On the Natural Focal Distribution of the Tick Relapsing Fever in the Turkoman Soviet Socialist Republic.**] *Med. Parasit. & Parasitic Dis.* Moscow. 1945, v. 14, No. 3, 56–9, 1 fig. [In Russian.]

The author notes that within the territory of the Turkmenistan the vectors of tick-borne relapsing fever are represented by three species of *Ornithodorus*. The most important and widely distributed of these is *O. papillipes* ; the second is *O. nereensis*, a new species described by the author, which lives in burrows and under stones but does not occur in human dwellings, while the third, *O. tartakovskyi* was found in the burrows of rodents. These ticks are occasionally found to be spontaneously infected with spirochaetes of gerbils (*Rhombomys*

opimus) in the valley of the river Murgab. To distinguish this spirochaete from the causative organism of human relapsing fever in Middle Asia (*Spirochaeta sogdianum*), it was named *S. latyschevi*.

In spite of the presence of these three vectors, tick-borne relapsing fever occurs in Turkmenistan only in rare sporadic cases, whereas it is much more common in Uzbekistan and in Tadjikistan. This is due to the fact that *O. papillipes* is a rare species in Turkmenistan, while *O. nereensis* and *O. tartakovskyi* inhabit biotypes with which man does not, as a rule, come in contact.

The author describes the case of two men who had taken shelter in a cave near Ashkhabad, and who developed relapsing fever nine days later, after showing typical traces of tick bites on the skin. An examination of the cave revealed ticks, *O. papillipes*, with a natural infection of spirochaetes. These facts point to the cave as a natural focus of tick-borne fever, which is probably primarily a disease of lower animals (zoonosis) upon which the ticks feed.

C. A. Hoare.

SOFIEV, M. S. & LEONOVA, N. A. [**New Data on the Reservoirs of the Virus of Tick-borne Relapsing Fever in the Uzbek Soviet Socialist Republic.**] *Med. Parasit. & Parasitic Dis.* Moscow. 1945, v. 14, No. 3, 60–65, 1 fig. [In Russian.]

This paper is devoted to a study of the reservoir hosts of tick-borne relapsing fever in Fergana (Uzbekistan). Previously the following animals have been found, in Middle Asia, to be naturally infected with spirochaetes of relapsing fever: dogs, rats (*Rattus turkestanicus*), gerbils (*Rhombomys opimus* and *Gerbillus eversmanni*), bats (*Rhinolophus ferrumequinum*) and mice (*Mus musculus severtzovi*). In Fergana the principal reservoir hosts were found to be mice, 6 per cent. of which proved to be naturally infected. The duration of the disease in these rodents is 12–28 days, and it is thought that in the course of the summer, probably all the mice became infected. In view of their constant migrations, it is suspected that mice serve as carriers of infected ticks (*Ornithodorus papillipes*) from house to house, thus serving to disseminate relapsing fever. Experimental infections with spirochaetes obtained from mice proved that they were identical with the spirochaete isolated from man.

As regards the spirochaetes of relapsing fever in gerbils (of which up to 17 per cent. are naturally infected), these differ from the human strains in various biological characters (*e.g.*, virulence for guineapigs), and have a distinct vector, *O. tartakovskyi*, on account of which they are regarded as an independent species, *S. latyschevi* Sofiev, 1941.

C. A. Hoare.

PAVLOVSKY, E. N. & KUZMINA, L. A. [**On the Possibility of Transmission of Spirochaetes of Tick-borne Relapsing Fever to Monkeys and to Man by the Tick** *Ornithodorus lahorensis.*] *Med. Parasit. & Parasitic Dis.* Moscow. 1945, v. 14, No. 3, 66–70, 1 fig. [In Russian.]

In view of some doubt regarding the part played by the tick, *Ornithodorus lahorensis*, in the transmission of relapsing fever in Persia, the authors have investigated this question experimentally, by feeding these ticks on infected monkeys and by allowing ticks fed on infected guineapigs to bite human beings. In all cases evidence of infection with spirochaetes was tested by direct examination and by inoculation of susceptible animals. None of the ticks which had fed on the blood of two baboons harbouring numerous spirochaetes became infected, while two patients suffering from general paralysis, who were bitten by ticks previously fed on guineapigs harbouring numerous

spirochaetes, likewise failed to acquire an infection. It is concluded from these and previous experiments that *O. lahorensis* is not a vector of relapsing fever. *C. A. Hoare.*

TROITSKY, N. V. [**Transmission of the Tick-borne Spirochaetosis by the various Stages of** *Ornithodorus papillipes.*] *Med. Parasit. & Parasitic Dis.* Moscow. 1945, v. 14, No. 3, 70–75. [In Russian.]

In the course of its metamorphosis, the chief vector of tick-borne relapsing fever in Middle Asia, *Ornithodorus papillipes*, passes through one larval and from three to five nymphal stages. In each stage the ticks feed at least once on some vertebrate animal. From 20 to 50 or more days after feeding, the tick moults and is transformed into the next stage of development. After moulting, nymphs of the last stage become adult males or females, which feed repeatedly but do not moult.

The author records the results of experiments carried out to determine the ability of different stages of the tick to transmit spirochaetosis. The ticks used in these experiments were collected from a disused and dilapidated piggery, and repeated examination of random samples failed to reveal any natural infection among them. Guineapigs were used both as the source of infection of ticks and to test the infection in the latter.

It was demonstrated that all the stages of development of *O. papillipes*, from larva to sexually mature imago, were capable of acquiring an infection by ingesting blood containing spirochaetes. They were all capable of retaining the spirochaetes in the successive stages of their development, and of infecting susceptible animals by bite. Moreover, it was shown that the spirochaetes can be transmitted hereditarily through the ova of the ticks, which is an important epidemiological factor. After having fed on blood containing spirochaetes, the ticks are capable of transmitting the infection by bite only after the expiration of a certain interval of time, which varies with the stage of development: in sexually mature adults it is from one to two months, while in larvae and nymphs the interval is determined by the time of ecdysis. Several days after the infective feed, the number of spirochaetes in the body of the tick gradually diminishes until it becomes very small, thenceforth remaining at a low level. *C. A. Hoare.*

TROITSKY, N. V. [**Experiments on the Application of Carbon Disulphide, Chloropicrine, K-Soap and other Insecticides for destroying and repelling the Ticks** *Ornithodorus papillipes.*] *Med. Parasit. & Parasitic Dis.* Moscow. 1945, v. 14, No. 3, 75–9. [In Russian.]

The author notes the importance of *Ornithodorus papillipes*, as a vector of tick-borne relapsing fever in Middle Asia, where up to 100 per cent. of the population in endemic areas are affected. The existing methods of destruction of the tick are unsatisfactory, mainly owing to the inaccessibility of its habitats (cracks in the walls of houses, fine sand or dust in caves, etc.) and also because of the absorption of the insecticides by the substratum. In the present paper an account is given of the results of tests on the effect upon these ticks of various chemicals, which were tested both for their lethal and repellent properties.

For lethal tests, the ticks were placed in jars or in desiccators, with a layer of sand or soil, into which they burrowed themselves. In the case of chloropicrin, about 100 cc. per cubic metre, acting for five to six hours, were required to kill the ticks. Paradichlorobenzene in a dosage of 250 cc. per cubic metre killed all the ticks only after 30 to 36 hours. The best results were obtained

with carbon disulphide, which killed the ticks in a dosage of 250 cc. per cubic metre after exposure for 24 hours. It is concluded that the most practicable method for tick-infested buildings is the successive treatment with two insecticides. First, with carbon disulphide, the fumes of which rapidly fill the room and can be eliminated after six to twelve hours; and second, with paradichlorobenzene which, when placed in suitable positions, prevents fresh infestation of the building.

As regards repellents, the following were tested:—Paradichlorobenzene, "N.C.I." (naphthalene 94 parts, creosote and iodoform, 3 parts each, which were made into a 5 to 10 per cent. solution in petrol), menthol, soap "K" and tar preparations. These were tested on guineapigs, which were either powdered with the preparation or clothed in an overall soaked in a solution of the preparation. None of these tests gave completely satisfactory results.

C. A. Hoare.

LEONOVA, N. A. [**On the Possibility of Transmission by Lice of the Spirochaetes of Tick-borne Relapsing Fever,** *Sp. uzbekistanica* (=*Sp. sogdianum*). *Med. Parasit. & Parasitic Dis.* Moscow. 1945, v. 14, No. 3, 79–82. [In Russian.]

The author describes the results of experiments designed to test the viability of spirochaetes of the Middle Asia type of tick-borne relapsing fever in the body-louse, and the possibility of their transmission by this insect.

In two series of experiments, lice, collected on human beings and bred in the laboratory respectively, were allowed to feed on mental patients infected with *Spirochaeta uzbekistanica* for therapeutic purposes. The results were assessed (1) by emulsifying the lice and injecting the emulsion into guineapigs, and (2) by examining the intestinal contents of the lice under dark-field illumination and in stained smears. In a third series of experiments lice were inoculated by Weigl's method, with citrated blood of a guineapig containing numerous spirochaetes. The lice were subsequently dissected and their intestinal contents were examined microscopically under dark-field illumination.

In all of these experiments the results were consistently negative. It was demonstrated that the spirochaetes lose their viability several hours after inoculation into lice, which are incapable of transmitting the infection to guineapigs.

C. A. Hoare.

DESPORTES, C. & CAMPANA, Y. Sur *Ornithodorus tholozani* (Laboulbène et Mégnin 1882) et sur les ornithodores de l'Asie centrale et mineure. [*O. tholozani* **and other Ticks of the same Genus in Central Asia and Asia Minor.**] *Ann. Parasit. Humaine et Comparée.* 1946, v. 21, Nos. 1/2, 74–88, 3 figs. [19 refs.]

ZARAFONETIS, C. J. D., INGRAHAM, H. S. & BERRY, J. F. **Weil-Felix and Typhus Complement-Fixation Tests in Relapsing Fever, with special reference to** *B. proteus* **OX-K Agglutination.** *J. Immunology.* 1946, Mar., v. 52, No. 3, 189–99, 1 chart. [12 refs.]

Weil-Felix and typhus-complement-fixation tests were carried out on sera of 50 patients under treatment for louse-borne relapsing fever in a Cairo hospital. The diagnosis was confirmed in every case by finding spirochaetes.

Proteus OXK was agglutinated, usually in rising titre, in every case. In 9 patients the maximum titre of complete agglutination that was observed was 1–40; in 11 it was 1–80; and in 30 it rose to 1–160 or over. Titres ranging from 1–640 to 1–2,560 were observed in as many as 14 of the patients.

Among 351 patients suffering from typhus, typhoid fever, smallpox, and

other diseases the positive reactions with *OXK* were :—27 at 1–40, 7 at 1–80, and 4 at 1–160.

Among the relapsing-fever patients there were two who reacted at high titres with the *OX19*-agglutination and the typhus-complement-fixation tests, and who presumably had typhus fever as well as relapsing fever ; apart from these only one relapsing-fever patient reacted with either of these tests at a titre higher than 1–80, and in his case the typhus-complement-fixation reaction remained constant at 1–160 on the 2nd, 9th and 15th days.

The author mentions the findings of ELSDON-DEW who observed *OXK* titres of 1–100 or over in 211 of 650 patients suffering from louse-borne relapsing fever in Ethiopia [this *Bulletin*, 1944, v. 41, 486].

From the table it appears that the maximum *OXK* titre in the authors' relapsing fever patients was usually reached by the end of the second week, though in a few cases the titre continued to rise during the third week.

John W. D. Megaw.

MARTÍNEZ BÁEZ, M. & VILLASANA, A. Sobre la histopatología de la fiebre recurrente experimental. [**The Histopathology of Experimental Relapsing Fever.**] *Rev. Inst. Salubridad y Enfermedades Trop.* Mexico. 1945, Sept., v. 6, No. 3, 185–94, 10 figs. [14 refs.] English summary (2 lines).

The brains of 15 white rats, infected by subcutaneous injection of *Spirochaeta novyi*, were examined microscopically ; 8 were killed during the febrile attack and the other 7 at various times from a day to two months after the end of the attacks, when no spirochaetes could be found in the blood.

In rats killed during the febrile attack, there was intense congestion of the vessels of the pia mater and of the cerebral capillaries ; in 3 rats recent haemorrhagic foci, 1–2 mm. in diameter and of varying depth, were seen in the cortex, and at the margins of these haemorrhages spirochaetes were very numerous. Spirochaetes were found also in the cerebral capillaries, the vessels of the pia mater, the choroid plexuses, and the parenchyma of the brain. An intense microglial reaction was always present, especially in the cerebral and cerebellar cortex, and in the cornu ammonis. No changes were observed in the nerve cells and no reaction in the neuroglia.

In rats killed later, no old haemorrhages were seen and it is suggested that they had been absorbed. No special pathological lesions were seen except discrete lymphocytic infiltrations in the pia mater.

The paper is illustrated with ten photomicrographs. *J. F. Corson.*

MUWAZI, E. M. K. **Penicillin in Treatment of Relapsing Fever.** *East African Med. J.* 1946, Feb., v. 23, No. 2, 55–64.

A record of the treatment of 37 cases of African tick fever (*Spirochaeta duttoni*) at the Mulago Hospital, Uganda, carried out in order to compare the therapeutic efficiency of penicillin and arsenicals.

The patients were divided into three groups. Eleven patients were treated with sodium penicillin in doses ranging from 100,000 Oxford units in 24 hours to 900,000 units in 72 hours. Five of them relapsed, and one had seven relapses. It is also of interest that several patients in this group were not without symptoms such as headaches and limb pains during the intermissions.

Eight patients were used as control and treated with a single dose of 0·6–0·9 gm. of neoarsphenamine (N.A.B.) injected intravenously. Five of them relapsed and two showed five relapses each.

Eighteen patients were treated with total doses of from 100,000 to 900,000 units of penicillin in 24 to 72 hours, combined with single maximum doses (0·75–0·9 gm.) of N.A.B. Seven relapsed and one patient had four relapses.

The author remarks that it is difficult to assess the therapeutic efficacy of penicillin, since natural recovery occurs in a high percentage of cases of relapsing fever. Moreover, the initial fever is not prolonged and the apyrexial intervals are of very irregular duration, which, combined with the difficulty of controlling the patients, made it almost impossible to follow up the cases adequately.

The results indicate, however, that neither penicillin nor N.A.B. either alone or in combination, is effective in preventing relapses in African tick fever. Both of them shorten febrile attacks, but neither is an effective remedy, which has yet to be discovered. *E. Hindle.*

SCHUHARDT, V. T. & HEMPHILL, Emmarie C. **Brain Involvement as a possible Cause of Relapse after Treatment in Spirochetal Relapsing Fever.** *Science.* 1946, Apr. 5, 422–3.

A discussion of the results of experiments on the treatment of rats infected with a strain of relapsing fever transmitted by *Ornithodorus turicata*, by means of penicillin sodium administered both intraperitoneally and intracranially [see this *Bulletin*, 1945, v. 42, 735].

A total of 53 rats were infected with similar doses of blood containing spirochaetes, and penicillin therapy was begun on the second or third day after their blood became positive. Twenty-five rats were each given 1,000 units of penicillin in a single intracranial injection and the 23 survivors received 1 to 14 intraperitoneal injections of penicillin at 3-hour intervals in doses ranging from 4,400 to 50,900 units per kgm. body weight. Nineteen rats were treated by intraperitoneal injections alone, and nine were kept as untreated controls. All these nine were brain positive when tested 31 days later.

The total of 27 treated rats which received less than 40,000 units/kgm. all relapsed, regardless of whether they received intracranial injections or not. The relapse and positive brain infections of the 13 rats receiving intracranial injections are interpreted as the result of inadequate therapy to cure the infection in blood or visceral tissues. Fifteen rats received more than 40,000 units/kgm. and 10 of these intracranial penicillin. Of the latter, 6 received only 4 injections and 3 showed positive brain infections possibly as the result of adhering infected blood; the other 4 rats remained negative, including brain passages, after 31 days.

The 5 rats receiving no intracranial injections all relapsed or showed positive brain infections.

The results support the view that after intraperitoneal treatment, relapses may occur as the result of spirochaetes re-entering the blood after persistence in the central nervous system. *E. Hindle.*

BOK, R. Het voorkomen van de rattebeetspiril in de oorspeekselklier van de muis. [**The Presence of** *Spirillum minus* **in the Ear Salivary Glands of Mice.**] *Acta Leidensia* (*Scholae Med. Tropicae*). 1940–41, v. 15–16, 143–51. [12 refs.] English summary.

"Many weeks after the infection the causative agent of rat-bite fever is found in larger numbers in the ear salivary glands of mice than in their blood. This speaks in favour of a possible rôle of the saliva in the transmission.

"The author has not succeeded in demonstrating the organisms in sections of salivary glands and other organs. So she doubts the exactness of the researches of KUSAMA, KOBAYASHI, KASAI and others, who might have taken nerves for Spirilla."

NITTI, F., CONGE, M. & KAUFFMANN, G., Mlle. Traitement du sodoku expérimental du cobaye par de faibles doses de penicilline. [**The Treatment of Experimental Rat-Bite Fever in the Guineapig with Small Doses of Penicillin.**] *Ann. Inst. Pasteur.* 1946, Mar.–Apr., v. 72, Nos. 3/4, 294–5.

Few guineapigs were available, and only small quantities of penicillin, but four experiments were made with daily doses of 600 to 1,000 units per kgm.; in each experiment and in every guineapig treated, the spirilla disappeared from the blood, and in some cases the animals ceased to lose weight. Relapses occurred after 4 to 30 days according to the dosage of penicillin given, and the animals died. The authors think that at least a certain proportion of cures may be hoped for with the use of larger doses. [See also LOURIE & COLLIER, this *Bulletin*, 1944, v. 41, 293.] *J. F. Corson.*

LEPROSY.

CERRI, B. Ricerche sul sangue e sul midollo sternale nella lebbra. [**Studies of the Blood and Sternal Marrow in Leprosy.**] *Haematologica.* Pavia. 1942, v. 24, Nos. 3 & 4, 167–244; 269–334, 12 figs. (2 coloured) & 6 graphs. [47 refs.] French summary.

Not all of this long article is taken up with the subject as stated in the title. For example, several pages are given to the history of sternal puncture and its uses in venereal and cutaneous diseases, including syphilis and Kaposi's disease, which have nothing to do with leprosy. On the other hand, the author includes other matters concerned with leprosy, such as the results of biopsy of the skin and of examinations of the nasal mucus.

For his specific purpose the author took blood from the finger-tip and marrow from the sternum, both in the morning of the same day, and also material from the nasal mucus and from puncture of an inguinal lymphatic gland and, when the patient consented, of biopsy material from a leprotic lesion. For examination, the methods of staining were the May-Grünwald-Giemsa and the Ziehl-Neelsen.

The patients comprised 23 with the nodular type of disease, 11 with mixed leprosy, and one with the nervous form. Details of each of the 35 are given, in letterpress and in tables; the examinations were very full. Of the blood, estimations were made of the haemoglobin, the number of red and white cells, and a differential count of 400–500 of the latter. The examinations of the marrow were much more exhaustive; 20 varieties of cells were counted and their relative percentages calculated. [We have checked the first ten of these tables and in one instance only does the total come to 100 per cent.; all the others exceed this, ranging between 102·2 and 110·6 per cent. The percentages in the blood counts are more often correct.] Leucopenia of 2,600 and 4,150 respectively was found in two cases, the one in the nodular group, the other in the mixed leprosy group. Leucocytosis up to 14,850 per cmm. was found in five, 2 of the first group (nodular cases), and 3 of the second (mixed). Another of the first group, during a leprous reaction, had a leucocytosis of 26,900 per cmm. Anaemia was a constant feature, nearly always hypochromic, with some degree of anisocytosis and, rarely, poikilocytosis; neutrophil metamyelocytes were also always present but not in large numbers; "non-segmented neutrophiles" were more common, up to 35 per cent. of the neutrophiles.

In the marrow, points specially noted were asynchronism of maturation of cells, asymmetry, fusion of chromosomes, pyknosis and staining irregularities. In general the marrow showed abundance of worn-out cells, scarcity of areolar tissue and of vacuolated cells ; activity in production of granuloblasts, raised leuco-erythroblast ratio and increased karyokinesis, increase of myelocytes and metamyelocytes, and predominance of erythropoiesis over leucopoiesis ; lymphocytes and monocytes showed a moderate increase, eosinophiles generally below normal ; haemocytoblasts and histiocytes variable, but on the low side. In general, the marrow presented signs of degeneration of cells and departure from the normal in size, relative proportion of nucleus to protoplasm, of " over-granulation " with atypical forms and staining affinities, and atypical also in the number of nuclei in the granulocytes, and polychromatophilia with basophilic granulations in the erythrocytes.

In the material obtained by puncture of the inguinal glands the author noted cells of varied size, sometimes " very large " [size not stated], with a histioid or monocyte nucleus, the protoplasm basophilic with acidophile particles, with clean-cut edges and vacuolated ; also typical plasma cells, some binucleate, and Türck's cells.

Biopsy specimens were obtained from five patients and from four material from scarification of lepromata ; there was nothing calling for special mention in these.

Examination for bacilli of leprosy in the marrow, gland-juice, skin and nasal mucus may be summarized as follows : They were found in all four situations in six of the patients and all were in the first group of nodular cases. In the marrow smears in 16 of the first group, three of the second (mixed leprosy), not in the nerve-type patient. The last may be disposed of in a few words ; the skin was not examined, but no bacteria were found in any of the other situations. As regards the gland-puncture results : In the 23 of the nodular group, Hansen's bacteria were seen in 17, few in some, numerous in others, sometimes singly, sometimes in masses ; five were not examined by gland-puncture and in one of those examined none was found. In the second group of 11, they were found in five and not found in three ; three were not examined. The skin was examined in nine of the first group only and infection was present in all. The nasal mucus was negative in three of the first group, positive in the other 20 ; negative in two, positive in nine of the second group ; absent, as already stated, in the " nerve " case. *H. Harold Scott.*

SHLIMOVITZ, N. **Leprosy : a Report of Nine Cases among Natives of the Mount Hagen Area in New Guinea.** *Med. J. Australia.* 1946, Mar. 16, v. 1, No. 11, 369–70, 4 figs.

This is an illustrated account of leprosy cases found in the mountainous interior of New Guinea at an elevation of 5,000 feet, where the disease had not previously been reported. It is, however, well known in the low coastal areas, in which there was a leprosarium at Mandang. Some of the cases are of long standing, and the disease, therefore, is not of recent importation. Three of the patients showed advanced neural signs, with the development of claw hands ; three more were earlier neural cases with discoloured patches and alterations of sensation. Another showed thickened ulnar nerves, without deformity of the hands, but with a few ulcers about his ankles. The remaining two were lepromatous cases ; one showed large nodules containing numerous lepra bacilli, and the other involvement of the nose and larynx. Arrangements for isolation of these patients are being considered, and it is stated that leprosy undoubtedly exists in other localities in the interior of New Guinea.

L. Rogers.

ARNOLD, H. L., Jr. **Differentiation of Lepromatous from "Neural" Leprosy. The Basis, a Method, and Report of Five Cases.** *Arch. Dermat. & Syph.* 1945, Nov.–Dec., v. 52, No. 5, 354–64, 7 figs. [Refs. in footnotes.]

This is a useful and up-to-date paper by an experienced worker in Hawaii on the diagnosis of the types of leprosy as a basis for prognosis and preventive measures. The author deprecates the use of the term "mixed leprosy", in that it is not applied to a mixture of the main lepromatous and neural types, but really means that the sites of involvement—both skin and nerves—by the lepromatous forms, are mixed; for in nearly every case of leprosy lesions of both the skin and the nerves are found. Lepromatous cases are characterized by the presence of raised red patches or diffuse granulomatous infiltration of the skin, rich in *Mycobacterium leprae*, and in advanced cases many of the internal organs are involved; nerve trunks are also implicated, with resulting paralyses and loss of sensation of the extremities. The eyes, nose and larynx suffer severely in late cases, and chronic nephritis and amyloid disease of the organs are important complications. The skin lesions can be differentiated from the tuberculoid variety of neural leprosy only by microscopical examination, which shows round and spindle-shaped histiocytes loaded with the causative bacilli and with fat. The nerve trunks show very similar changes. The lepromin test is negative, and the sedimentation rate increased. Lepra fever occurs at times, with exacerbation of the symptoms and the appearance of new lesions resembling erythema nodosum; the prognosis is bad. On the other hand, in neural leprosy, small superficial nerves are involved in relation to skin lesions showing tuberculoid changes, but containing extremely few, scattered, bacilli; local discoloration of the skin and changes in sensation are found. The microscopical characters of these lesions are shown in illustrations. Prognosis in neural cases is comparatively good, and spontaneous recovery may ensue; they seldom require to be isolated. Isolation, however, is necessary in all lepromatous cases except very early ones. *L. Rogers.*

FITE, G. L. & GEMAR, F. **Regressive Changes in Leprosy under Promin Therapy.** *Southern Med. J.* 1946, Apr., v. 39, No. 4, 277–82, 1 fig.

This important paper records the results of the use of promin in the treatment of leprosy, over a period of four years. Daily intravenous doses, usually of 5 grammes, have been given over periods of three weeks, with an interval of one week between the courses. In some cases this treatment was continued for more than 4 years, with beneficial results in nearly all. Clinical improvement is slow and reduction in the number of lepra bacilli still slower, but progress is nearly always steady, and relapses or febrile exacerbations very rare. Repeated microscopical examinations of the skin lesions showed disappearance of inflammatory signs and diminution in the number of bacilli, but the latter often did not disappear completely, although typical cigar-like packets of organisms became extremely rare. The greatest decline in the number of organisms was seen during the fourth year of treatment, by the end of which they had disappeared from 21 of 42 patients. With one exception the skin lesions showed extensive evidence of atrophy. The deeper foci of infection showed the greatest diminution in size and in the number of bacilli; this may be due to the fact that there is a better blood supply at these sites, which brings the drug into closer contact with the bacilli. The lipoids in the affected tissue remain undiminished, and many vacuolated fatty cells persist. Fibrosis is not a feature of regressive lesions.

The drug appears to act by ridding the blood vessels of lepra bacilli and so preventing their spread throughout the body to form new and progressive

lesions. There is little evidence that promin destroys the bacilli in the tissues, but they gradually decrease in the old lesions in accordance with the self-healing tendency of leprosy. This explains the slowly beneficial action of the drug. The absence of acute reactions strongly suggests the destruction of the organisms in the blood and the prevention of their dissemination through the body as the essential action of this treatment, and their gradual reduction in the tissues to the point of final disappearance, as was observed in 10 out of 32 cases treated for four years. A still more powerful bactericidal agent is required for the chemical destruction of bacilli within the tissue cells, and especially in the globi laden with the organisms. Chemotherapeutic research with drugs of allied composition seems most likely to furnish this requisite.

L. Rogers.

DE WILDEMAN, E. A propos de médicaments antilépreux d'origine végétale. V. Des "Ephedra" et de leur constitution chimique. [**Drugs of Vegetal Origin used in Leprosy. The Chemical Composition of Derivatives of** *Ephedra.*] *Inst. Roy. Colonial Belge—Bull. des Séances.* 1945, v. 16, No. 2, 396–412. [Refs. in footnotes.]

The author first discusses the history of the study of plants of the genus *Ephedra* in different parts of the world; these plants yield ephedrine and closely allied alkaloids, which are used chiefly in the treatment of asthma, but have occasionally been tried in leprosy. Thirty-one botanical varieties are enumerated in alphabetical order, with brief notes of work on those which have been investigated, and suggestions that have been made for their medicinal use. Drugs of this series have been used in China for many centuries, but varieties are met with in India, North Africa and America. Mention is made that preparations from these plants have been used in leprosy, but no evidence is given relating to results obtained, regarding which the author states that it is difficult to form any conclusions. This paper has, therefore, little medical interest.

L. Rogers.

HELMINTHIASIS.

ALVES, W. **The "Public Health Cure" of Bilharziasis with One-Day Course of Antimony.** *South African Med. J.* 1946, Mar. 23, v. 20, No. 6, 146–7.

A modified form of the intensive treatment of bilharziasis devised by the author [this *Bulletin*, 1945, v. 42, 815] and by ALVES and BLAIR [this *Bulletin*, 1946, v. 43, 344] is described in this paper.

A group of 131 Africans bilharzia-positive by a cercarial antigen skin test was divided into three groups, each of which was treated under a different dosage scheme, with sodium antimonyl tartrate by the slow-injection method previously described, as follows :—

Group A : 6 grains sodium antimonyl tartrate (S.A.T.) in three doses of 2 grains at four-hourly intervals.
Group B : 7½ grains S.A.T. in three doses of 2½ grains at four-hourly intervals.
Group C : 8 grains S.A.T. in four doses of 2 grains at three-hourly intervals.

The treatment thus occupied only one day. No marked reactions occurred, nor was there any obvious difference between the groups receiving different doses.

The S.A.T. solution was prepared as follows :—

Tap water	... ...	2,000 cc.
Glucose B.P.	... ...	100 grammes
Sodium chloride A.R.	...	17 grammes
S.A.T. powder B.P.	...	q.s. to make either 2 grains or 2½ grains per 10 cc. solution

" Dissolve, filter through paper, and autoclave at 120°C. for 20 minutes in 3,000 cc. flasks. Distribute under sterile conditions into sterile ' vacoliter ' bottles fitted with two-hole rubber stoppers. Seal stoppers with 6-in. squares of previously boiled, thin oilskin—similar to ' jaconet '—and tie down. Store in cold room at 4°C.

" The used ' vacoliter ' bottles would not stand autoclaving when filled, but were sterilised without damage in the hot-air oven at 160°C. for one hour. Hence the necessity for autoclaving the solution in flasks and transferring it. The rubber stoppers were boiled with the oilskin squares.

" For use, the oilskin covering a hole in the rubber stopper was wiped with alcohol and pierced with a syringe-needle, and the tip of the syringe (minus needle) was inserted, when 10 cc. could readily be withdrawn. The hole was then covered with sterile cotton-wool soaked in alcohol.

" Ten cc. of the solution contained either 2 grains or 2½ grains of S.A.T., and no further manipulation was necessary.

" These solutions were used up to seven weeks after their preparation and storage, and there was no evidence of deterioration to toxic material.

" The drug cost of treatment was ¼d. per patient."

Urines and stools of every patient were examined two weeks and four weeks after treatment. Seven were passing a few dead eggs on the first examination and one on the second examination, but in none were living eggs found.

The significance of this treatment lies in the fact that it provides a rapid method of disinfecting an infected population for a time at least, which, if used in conjunction with snail destruction, should prove to be a valuable weapon in anti-bilharzial campaigns. *J. J. C. Buckley.*

CAIRO : MINISTRY OF PUBLIC HEALTH. MEDICAL AFFAIRS. **Annual Report of the Bilharzia Snail Destruction Section 1943** [BARLOW, C. H. (Expert) & ABDEL AZIM, M. (Director). 27 pp., 3 maps (2 folding), 2 diagrams & 1 graph. 1946. Cairo : Govt. Press.

This report consists mainly of an account of the activities of the Snail Destruction Section during 1943 and the first part of 1944.

The methods of snail eradication, which are summarized briefly, remain essentially the same as those described in the 1942 report [this *Bulletin*, 1945, v. 42, 1017] and consist of a preliminary survey of canals and drains to note the location and numbers of snails, which is followed by treatment of the infested parts by means of (*a*) clearance of weeds and snails by mechanical methods such as nets, diggers, manual labour, and (*b*) sulphation by means of copper sulphate.

The progress of the campaign in Fayoum Province is reported upon and its success is indicated by a comparison of the 1942 ratio of the number of infested streams to the number surveyed, with the same ratio in 1943. This shows a reduction from 25 per cent. to 12 per cent.

The Fayoum campaign was succeeded late in 1942 by a similar one in Giza Province. The topography of this area is described, and for the purposes of

survey and treatment the province was divided into 14 areas, 11 on the west and 3 on the east of the Nile. In 1943, 4,111 streams were surveyed and 1,616 (39 per cent.) were found to be infested with snails. In 1944, after treatment, the percentage of infested streams fell to 22 per cent. The results of the work are also expressed by an estimation of the snail populations in infested streams before and after treatment. Thus, before treatment, 13,698 *Bulinus truncatus* were collected by dipping in infested streams [presumably with the standardized collecting nets described in the previous report]. This number represents an average of 63 snails in 100 dips. After treatment the average fell to 37 snails per 100 dips. Only two of the 14 areas were infested with *Planorbis boissyi*. The average number of this species per 100 dips was 125 before treatment and five after treatment.

Concerning the Dakhla Oasis, the field of a series of anti-bilharzial measures between 1926 and 1935, some comments are made upon the results of a mission which revisited this area in 1943.

A summary of the results of research work having a bearing on snail destruction is included in the report, and is described under the four headings: (1) Seasonal variations in the snail population of the fresh-water streams of Egypt. (2) Observations on the distribution of *Bulinus* and *Planorbis* snails during the winter closure 1943–1944. (3) Palm leaf traps in main canals and drains. (4) Random examination of *Bulinus* and *Planorbis* snails for schistosome infection in Giza Province.

A comprehensive map illustrates the scope of a projected 6-year plan for snail eradication along the course of the Nile, from Asswan down to and including the delta. *J. J. C. Buckley.*

VERSIANI, V., MARTINS, A. V. & SOBRINHO, O. P. Esquistossomose mansônica no estado de Minas Gerais. I.—Município de Belo Horizonte. [**Infestation with** *Schistosoma mansoni* **in the State of Minas Geraes.**] *Arquivos do Inst. Químico-Biol. Estado de Minas Gerais.* 1945, v. 1, 71–90, 3 figs. [26 refs.] English summary.

The existence of *S. mansoni* infestation in Minas Geraes has been known for more than a quarter of a century. The authors have lately examined the faeces of about 1 per cent. of the population of 36 municipalities in the State, choosing in particular children of school age, 7–15 years. The method utilized was to take about 2 gm. of the faeces in a Borel flask, emulsify with a little water and rapidly filter through a metal sieve of 80–100 meshes per sq. cm. into a conical glass; this was allowed to settle for 20 minutes. Fifty cmm. were then withdrawn with a pipette from the bottom of the sediment and examined under low power. Except for better identification of doubtful elements only one examination was made of each sample.

An average of 98 samples was obtained from each of 24 schools, 2,352 altogether; 294 or 12·5 per cent. were positive. Of 733 girls, 47 (6·4 per cent.), of the 1,619 boys, 247 (15·25) were positive. 1,234 were from whites and 142 (11·5) were positive among these; 331 were from blacks, 40 (12·08), and of 787 mulattos, 112 (14·23), were positive. Those of the poorest class were most infected, and the rate rose steadily with age, from 7·04 per cent. at 9 years to 25 per cent. at 15 years, the intermediate rates being 11·02, 13·13, 16·19, 17·42, and 23·45 per cent. Again, the highest infestation rate was in those living in rural zones. Thus, of 381 town-dwellers 33 were positive (8·6 per cent.), of 1,868 living in the suburbs 225 (12·04); of 103 rural 36 (34·9) were positive. *H. Harold Scott.*

OLIVEROS NAVA, B. Estudio estadistico del Servicio Antibilharziano de El Valle "Centro de Educación Sanitaria". [**Statistical Study of the Anti-Schistosomiasis Service in the El Valle District (Venezuela).**] *Rev. Sanidad y Asistencia Social.* Caracas. 1945, Oct.–Dec., v. 10, Nos. 5/6, 667–86, 5 graphs.

The author has analysed the histories of 1,358 patients suffering from infestation by *Schistosoma mansoni.* The commonest reasons for the patient applying for treatment were headache, dysenteric symptoms and abdominal pain, with general malaise; the chief symptoms were malaise and headache in 54–58 per cent. and "general debility" in 53 per cent. Blood and mucus in the stools were seen in only 14 per cent. Enlargement of the liver was present in 58 per cent., of the spleen in 63 per cent., but the latter was palpable in 15 per cent. only, the enlargement in the others being "by percussion" only [enlarged upwards ?]. More than half the cases (820, or 63 per cent.) occurred in El Valle, and 184 (14 per cent.) in El Tuy. Fifty other localities are mentioned, but generally few in each; only three had more than 50 and 12 had only two cases.

Treatment has been by tartar emetic, starting with 0·03 gm. The total dosage ranged between 1·2 and 1·8 gm. in 656 cases; 489 required a second course and 73 a third. Other drugs were tried, such as Neostan [? Neostam], Repodràl and Stibiamine [? Stibamine glucoside], but the numbers of patients to whom these were given are not stated, nor is there any mention of dosage. All that is said of them is that Repodràl has the advantage of being given intramuscularly and Stibiamine orally; Neostan is not referred to again.

H. Harold Scott.

MAGATH, T. B. & MATHIESON, D. R. **Important Factors in the Epidemiology of Schistosomiasis in Leyte.** *Amer. J. Hyg.* 1946, Mar., v. 43, No. 2, 152–63, 5 figs.

The authors attempted to evaluate the factors responsible for the spotty distribution of schistosomiasis in Leyte. They give an account of the ecology of the snail intermediary, *Schistosomophora* (*Oncomelania*) *quadrasi*, whose habitats are confined to certain types of water but have a wider distribution during some months in the year. Typically they inhabit the margins of slowly-moving water in small creeks where shade is abundant. They were not found in marshy land periodically flooded with sea water; in large rivers where the flow is rapid and the banks are sharply defined by steep sides without adjacent swamps; in ditches with impermanent water or water exposed to the sun; in stagnant water; nor in large, slow-flowing rivers.

The factors governing the localization of the disease were critically examined in Palo, a village of high endemicity. [The value of the detailed description of the topography of this place would be greatly enhanced by a sketch map.] The conclusions reached are that snails become infected mainly in the immediate neighbourhood of defaecation sites; that human infections may occur at any season, but that there may be a strong seasonal incidence; that the disease in Leyte is not occupational, but is essentially one of childhood; that of the reservoir hosts, pigs are more important in infecting snails than are dogs, and that wild rats are of little importance in this respect.

The determination of the exact type of water in which people may become infected is of great importance. Considerable space is devoted to a discussion of this problem and to the possibility of contracting the infection in large bodies of water; the trend of the authors' argument is against this possibility. [See also this *Bulletin*, 1945, v. 42, 1018; 1946, v. 43, 350.]

J. J. C. Buckley.

MAGATH, T. B. & MATHIESON, D. R. **Factors affecting the hatching of Ova of** *Schistosoma japonicum*. *J. Parasitology*. 1946, Feb., v. 32, No. 1, 64–8.

The functions of development and hatching in the case of *S. japonicum* eggs are very different, and are closely inter-related with the different physical environments which characterize the mammalian body and the exterior. While the eggs can develop at body temperature and in the normal salinity of the body, either of these conditions will prevent them from hatching. On leaving the body they are released from the influence of these inhibiting factors and hatch readily at the lower temperature and salinity usually encountered in tropical waters, if a third factor, a sufficiency of oxygen, is also present. The experiments described in this paper were designed to determine the factors which prevent *S. japonicum* eggs from hatching within the tissues or in the faeces of the definitive host.

It was found necessary to dilute the faeces with water until much of the putrescent material had been disposed of, to obtain a large hatch of miracidia. Hatching continued for several hours and then fell away when the water became foul. Active hatching was renewed when the water was aerated with a bicycle pump or a stream of oxygen. Observations on temperature effects showed that eggs remained viable but would not hatch up to 9 days at 18°C. The optimum hatching range was 25°C. to 31°C., and at higher temperatures it was inhibited. No hatching took place in the presence of sodium chloride concentrations as small as 0·7 per cent.

The miracidia were subjected to a gradually increasing temperature (0·5°C. per minute until 37°C. was reached) and it was noted that their most rapid motion was at 33°C. Thirty minutes' exposure to 37°C. was usually fatal. Two minutes' exposure to a 1·3 per cent. solution of sodium chloride was fatal, but the eggs survived for 1 hour in a 0·66 per cent. concentration, and after an hour in a 0·2 per cent. concentration they were apparently normal and might infect the snail intermediary. *J. J. C. Buckley.*

FAUST, E. C., WRIGHT, W. H., MCMULLEN, D. B. & HUNTER, G. W. **The Diagnosis of Schistosomiasis Japonica. I. The Symptoms, Signs and Physical Findings Characteristic of Schistosomiasis Japonica at Different Stages in the Development of the Disease.** *Amer. J. Trop. Med.* 1946, Jan., v. 26, No. 1, 87–112, 7 figs. [36 refs.]

Far Eastern schistosomiasis, Katayama disease, was first recognized in 1847; the clinical picture of the advanced disease was adequately described in 1883; and its causative agent was discovered in 1904. Japanese medical literature after 1883 contains much information on the aetiology, epidemiology, pathology, and attempted prevention of the condition, but there is little or no information on its incubation period and onset. In 1923 there was a report on a group of 40 Chinese boys and an adult American, who swam in infected water and were all ill, some seriously, one month later. Other outbreaks with less definite dating of the actual infection have been recorded by European and Chinese workers.

Several hundred cases of Eastern schistosomiasis occurred among American troops within a limited period of the invasion of Leyte Island in the Philippines (October 1944). A group of men in a R.A.A.F. construction squadron were also infected there. These two groups of cases were available to the authors for the study of the late incubation, the acute, and the early chronic stages of the infection. For the purpose of comparison, advanced chronic infections were available in natives in hospitals in Leyte and in Mindanao.

The factors governing the severity of the clinical manifestations of infection in the individual include :—(*a*) the intensity of available cercarial infestation

in the infecting water; (*b*) the gross area of skin, and particularly of mucous membrane, exposed to attack; (*c*) repetition of exposure to infestation; and (*d*) the reaction of the individual patient to the parasites. At the actual time of infection by the cercariae, needling sensations may be felt in the skin. A few days later there is an irritating, often unproductive, bronchial cough, which lasts for several days. Two weeks later moderate or severe urticaria may appear overnight, and the patient first appreciates that he is ill. Headache, mental dullness, tiredness and loss of weight, and a feeling of fullness and of pain on pressure over the epigastrium then develop; chills and sweats occur at night. These symptoms increase until some four to five weeks after the initial infection, when there is a sensation of fullness and pain in the right hypochondrium, general abdominal discomfort, mucous diarrhoea or a bloody dysentery, and marked loss of appetite.

The manifestations appear essentially in this order, but not all of them are usually encountered in each patient.

The acute stage of the disease sets in when the mature, fertilized female worms begin egg-laying, and the eggs appear in the stools within a few days. The acute stage lasts three or four months and then continues as the early chronic disease. Four types of the acute stage of Eastern schistosomiasis can be distinguished—(1) the fulminating, (2) the severe, with sudden onset, (3) the insidious, and (4) the asymptomatic. In type (1), the fulminating, death often occurs before a specific diagnosis is reached, and in the one case of this type seen by the authors, death occurred in spite of immediate antimony treatment begun before a parasitological diagnosis was made; an autopsy showed a massive parasitic infection, which had caused an overwhelming intoxication with the metabolites of the worms and their eggs.

In type (2), the severe with sudden onset, the appearances 4 to 5 weeks after infection are those of an undiagnosed fever, urticaria, angioneurotic oedema, gastrointestinal "distress", acute diarrhoea, dysentery, dengue, infectious hepatitis or an upper respiratory infection. Within 81 days of first infection, 61 per cent. of those found to be infected in one unit had been admitted to hospital, severely ill; 71 per cent. of these infected men had eosinophilia of over 30 per cent.; only 6 per cent. of them had eosinophilia of less than 10 per cent. and one patient had 90 per cent. eosinophilia. More detailed clinical accounts of these cases are to be published. Two new features, relatively common in these severe military cases, were "nuchal rigidity" (soreness and stiffness of the neck), and the development of "yellowish nodules" on the mucosal surface of the lower sigmoid colon and adjacent part of the rectum. The "yellowish nodules" were slightly elevated papillae, 1–3 mm. in diameter, which on scraping were found to contain eggs of *S. japonicum*.

In type (3), the insidious infections, a gradual development of symptoms and signs took place over a period of one to three months after the usual incubation period. Several such cases were seen in the military groups, and difficulty was experienced in diagnosis owing to the mildness of the manifestations. This was even more the case in type (4), asymptomatic infections, where the diagnosis was made by routine stool examinations.

The complications of Eastern schistosomiasis encountered were (*a*) extension of the lesions from the abdominal viscera to other organs and tissues of the body, and (*b*) secondary infections or disease processes. Extension of the lesions by the carriage of eggs to the lungs was seen in one case; in other cases eggs were transferred, by an unexplained mechanism, from the portal circulation to the systemic circulation, and lodged in end-arterioles of the toes, the skin, or the central nervous system. The complicating infections encountered included malaria, tuberculosis, amoebiasis, and other diseases of common occurrence in the tropics, all of which may obscure the clinical picture.

Passage into the early chronic form of the disease is due to the continued discharge into the body of metabolic products of the parasites, and the toxaemia resultant on their presence. The accumulation of the very large numbers of eggs produced by this species of fluke increasingly dominates the pathological picture, and those eggs which fail to reach the exterior act as foreign bodies, particularly in the intestine, the liver and the mesentery, with the resultant development of the classical changes associated with the advanced disease. Eighteen months to two years after initial infection the late chronic stage of the disease may develop in cases of very heavy infestation, but, more commonly, the onset of this stage is deferred for four or five years. In natives subject to repeated reinfection, manifestations of the early and the advanced stages are often coincident. In the military cases no significant chronic lesions were observed up to a year after infection ; these may be expected in untreated or inadequately treated cases in five to ten years' time.

The authors record in considerable detail the progress of Eastern schistosomiasis in the eight surviving members of a Filipino family infected in a newly-discovered endemic focus of infection in Mindanao ; and they go on to describe other indigenous cases in the same locality. Features of the Filipino cases were the absence of the " nuchal rigidity " so conspicuous in the American military cases ; the absence of significant eosinophilia at the times of examination ; and the absence of the severe and prostrating onset which characterized the majority of the American cases admitted to hospital.

The differential diagnosis of Eastern schistosomiasis is discussed.

[This paper contains much information and should be consulted in the original by those interested. See also this *Bulletin*, 1945, v. 42, 1018.]

A. R. D. Adams.

FAUST, E. C. **The Diagnosis of Schistosomiasis Japonica. II. The Diagnostic Characteristics of the Eggs of the Etiologic Agent** *Schistosoma japonicum. Amer. J. Trop. Med.* 1946, Jan., v. 26, No. 1, 113–23, 27 figs.

The typical, viable, mature ova of *Schistosoma japonicum* are readily identifiable, but, occasionally, plant cells in faeces are mistaken for " atypical eggs". A chain of eggs distends the venule in which they have been deposited by the retreating ovipositing female, which, while egg-laying, is grasped and held in position by the male worm. The newly-laid egg is immature, but normally matures rapidly, and the larva contained in it secretes an enzyme through the shell which aids in the escape of the ovum from the containing vessel, and in its migration through the tissues into the lumen of the gut. Back-pressure in the obstructed capillary, and the contractions of the bowel wall, contribute to this process. Immature or degenerate eggs, as well as mature eggs, may be passed in faeces, and their recognition may present difficulties. Descriptions, with camera-lucida drawings, are given of the wide ranges in size and shape and of the appearances of the immature and maturing eggs, of mature viable eggs, and of different types and stages of degenerate and dead eggs of *S. japonicum* voided in the stools of infected dogs and men. Careful search of the stools of infected persons by the skilled laboratory worker will usually be rewarded by the recovery of identifiable eggs, particularly if a concentration technique is employed. Even where they cannot be found, scrapings, through a proctoscope, from those cases with creamy or yellowish pinpoint nodules at or below the recto-sigmoid junction will yield a parasitological diagnosis. Where even this fails, if a diffuse intestinal capillary dilatation can be seen proctoscopically, attempted aspiration will rupture the wall of a capillary, and the microscopic specimen of blood which exudes may yield a few eggs.

A. R. D. Adams.

DESPORTES, C. La dermatite des nageurs. [**Swimmer's Itch.**] *Ann. Parasit. Humaine et Comparée.* 1944–1945, v. 20, Nos. 5/6, 263–78, 1 fig. [24 refs.]

During the prolonged dry period of October 1944, the author observed foci of snail-infested water at Indre-et-Loire. Twelve per cent. of these snails were emitting ocellated furcocercous cercariae. Voluntary exposure of the legs, on two occasions, in infested water resulted in a dermatitis, which is described in detail. The beneficial effect of cryotherapy [the use of cold] in alleviating the pruritus is recorded.

In the subsequent section of this paper the literature of "swimmer's itch" is reviewed and a general study of the disease is set down from the aspects of synonymy, definition, aetiology, pathogeny, geographical distribution, symptoms, clinical picture, histopathology, diagnosis, and individual and general prophylaxis. *J. J. C. Buckley.*

LARSH, J. E., Jr. **A Comparison of the Percentage Development of a Mouse Strain of *Hymenolepis* in Alcoholic and Non-Alcoholic Rats and Mice.** *J. Parasitology.* 1946, Feb., v. 32, No. 1, 61–3.

"Seven similar experiments were performed in which a comparison was made of the percentage development of *H. nana* var. *fraterna* in alcoholic and non-alcoholic rats and mice. In all but one experiment, the alcoholic rats showed percentages of cysticercoid development at least 2·4 times greater than those of non-alcoholic controls. At the same time, alcoholic mice had percentages at least 2·1 times greater than controls in every experiment. These results are interpreted to mean that most young rats as well as mice show a reduced natural resistance to *Hymenolepis* following repeated alcoholization."

LARSH, J. E., Jr. **The Effect of Alcohol on the Development of Acquired Immunity to *Hymenolepis* in Mice.** *J. Parasitology.* 1946, Feb., v. 32, No. 1, 72–8. [13 refs.]

"Experiments were carried out to determine the influence of 35 per cent. alcohol on reinfection of mice with *H. nana* var. *fraterna.* When daily treatment with the drug was not begun until several days after initial infection, it had no demonstrable effect on reinfection several weeks later. Thus the action of the immune mechanism stimulated before alcoholization was not interfered with in degree to be measured by the infection method employed. In other experiments in which the drug treatment was given daily for a few weeks before the first infection the results varied with the time interval before reinfection. When this period was one week or 72 hours, reinfection was not demonstrated. This probably meant that the alcoholic mice had recovered from debilitation. On the other hand, reinfection was demonstrated where only 48 or 24 hours elapsed between infections. In both cases the alcoholic mice showed percentages of cysticercoid development many times greater than those of controls. This indicated, therefore, that alcohol treatment caused a delayed response to antigenic stimulation but the mechanism for this is as yet unknown."

SANGSTER, C. B. **Hookworm Disease in Australian Soldiers, with Reports of Cases.** *Med. J. Australia.* 1946, Mar. 23, v. 1, No. 12, 385–93, 3 figs.

This is an account of hookworm disease among Australian soldiers in New Guinea during nine months in 1943–44, and in Bougainville island during the

first half of 1945 ; its chief interest is in the detailed description of three acute cases in Bougainville.

In New Guinea the disease was clinically mild and the diagnosis was usually indicated during examination of the blood for malarial or other parasites, or of the faeces for amoebae. In some cases the patient complained of lassitude, abdominal discomfort, dyspnoea on exertion and œdema of the ankles, regarded as signs of anaemia. The anaemia was normochromic and normocytic and the haemoglobin was rarely less than 11 gm. per 100 cc. The treatment was : oil of chenopodium 1 cc. together with either tetrachlorethylene 4 cc. or carbon tetrachloride 3 cc. ; this dose was repeated after 8 days if thought necessary. Ferrous sulphate, 3 gm. t.d.s., was given for anaemia. A good diet was supplemented in some cases with vitamins B_1 and C.

In Bougainville the disease was also usually mild but there were three acute cases, and some others gave the classical history of the symptoms of the invasive stage. *Ground itch*, usually erythematous and vesicular, was observed, in different patients, from a few minutes to a few days after contact with infected ground. *Cough* and *sore throat* with, in some cases, bloodstained sputum, appeared after 5 to 7 days and lasted for a month or more. *Abdominal discomfort* appeared from two to several weeks later ; anorexia, nausea, sometimes vomiting and cramps occurred and there was also intermittent diarrhoea, treated as for dysentery with sulphaguanidine without effect however. This history was given by 25 patients.

Diagnosis.—In Bougainville both *Ancylostoma duodenale* and *Necator americanus* were present, in New Guinea only *Necator americanus* was found. High eosinophilia was observed in blood examinations, an absolute count of over 400 per cmm. being regarded as significant ; the highest count was 51,000 (85 per cent.). Numerous eosinophils (50 per cent.) were also seen in the vesicular fluid of skin lesions, and the sputum also showed numerous eosinophils.

Acute cases.—These three cases are described in detail throughout the illness. There was severe anaemia, and persistent diarrhoea with a considerable amount of blood in the stools was present, though hookworm ova were not found for several weeks. Repeated doses of the anthelmintic mixture were required, and blood transfusions were needed, one patient receiving a total of over 500 ounces in 12 transfusions. This man had a mixed infection of *A. duodenale* and *N. americanus* while the other two had *N. americanus* only. One of the patients developed an abscess of the lung ; another was infested with about 3,500 hookworms. Examinations of the sternal marrow showed " no lack of maturation and no depression of the erythroblastic series." All three patients recovered after severe illnesses lasting several months. *J. F. Corson.*

DE MEIRA, M. T. V., GIRÃO, J. & COITO, A. de M. F. Sôbre um foco de ancilostomiase rural autóctona em Portugal. [**A Rural Focus of Ankylostomiasis in Portugal.**] *An. Inst. Med. Trop.* Lisbon. 1945, Dec., v. 2, 267–73. English summary.

KARTMAN, L. **A Note on Anopheline Vectors of** *Wuchereria bancrofti* **in West Africa.** [Research Notes.] *J. Parasitology.* 1946, Feb., v. 32, No. 1, 91–2.

During the early part [January to May] of 1944 the author dissected *Anopheles gambiae* and *A. funestus* caught in four native villages situated within 12 miles eastward of Dakar, Senegal, French West Africa ; the results are seen in the table.

TABLE 1.

W. bancrofti *in anopheline mosquitoes from four native villages.*

Date (1944)	Village	Host	Number Dissected	No. filaria found in					Number Infected	Per cent. Infection
				Gut	Abdomen	Thorax	Head	Proboscis		
1–15 to 5–17	A	*A. gambiae*	79	15	0	58	0	1	39	49·3
		A. funestus	351	24	0	63	0	0	65	18·5
1–21 to 5–17	B	*A. gambiae*	23	3	0	2	0	0	3	13·0
		A. funestus	82	0	0	2	0	1	2	2·4
1–17 to 5–15	C	*A. gambiae*	72	61	0	44	9	0	39	54·1
		A. funestus	223	26	0	18	0	0	41	18·3
5–30 to 6–16	D	*A. gambiae*	206	19	3	44	4	0	56	28·0
		A. funestus	90	2	3	7	1	0	9	10·0
Total		*A. gambiae*	374	98	3	148	13	1	137	36·6
		A. funestus	746	52	3	90	1	1	117	15·6

These two species were predominant throughout the year, far outnumbering all other mosquitoes, including *Culex fatigans*. The author states that it has been suggested that *A. funestus* has a lower infection rate than *A. gambiae* because, being a smaller mosquito, it takes less blood at a feed than *A. gambiae* does. *J. F. Corson.*

BEHM, A. W. & HAYMAN, J. M., Jr. **The Course of Filariasis after Removal from an Endemic Area.** *Amer. J. Med. Sci.* 1946, Apr., v. 211, No. 4, 385–94, 3 figs. [13 refs.]

A report on the condition of men from the American forces invalided with alleged filariasis from Tonga-tabu, an endemic area of Bancroftian filariasis, on their arrival in the United States in the latter part of 1943 has already appeared [this *Bulletin*, 1945, v. 42, 1020]. The present paper is an "interim report" on the progress of these men (Group A) two years later. It also contains information on a second group (Group B) of 145 men who were exposed to possible infection in Woodlark Island (off New Guinea), and on a further group (Group C) of 32 men who had never been in a filaria endemic zone. Woodlark Island lies in the filaria endemic zone, but there is no record of a native of the island having been shown to harbour the infection.

In the Tonga-tabu cases (Group A) parasites were demonstrated in very few men; other laboratory tests were unhelpful; and the diagnosis of filariasis was essentially clinical. In the 532 men comprising this group the authors consider that only 196 really had filariasis and that 336 were free from the infection. The intradermal test with a *Dirofilaria immitis* antigen proved of doubtful value in differentiating the uninfected from the infected, as false positive reactions were obtained even in the controls (Group C). A history of one or more attacks of "mumu" (fever, lymphadenopathy and retrograde lymphadenitis) with swelling lasting at least one day, was regarded as convincing evidence of an infection. Adenopathy alone was of little significance as it was extremely common in the forces in the Pacific islands. In infected persons the symptoms and signs decrease with the passage of time, and most of the infected Group A cases were free of symptoms 20 months after leaving the endemic area.

The authors analyse, in some detail, the clinical findings among the infected and the uninfected men in Group A, and compare them with those encountered in the 145 Group B men from Woodlark island, whose infection at best was problematical. They find a striking similarity in the clinical manifestations, such as swelling of limbs or the scrotum, and adenopathy, in the three groups. Owing to the fact that most physicians lacked acquaintance with the disease, a diagnosis of early filariasis was often made on quite inadequate grounds, even in men who could never have been exposed to infection. The psychological complications of the diagnosis are considerable in view of the (usually ill-founded) fears it engenders, and the lack of any specific treatment.

The longer an ill-founded diagnosis is allowed to continue, the greater the difficulty in restoring the patient to full normality. *A. R. D. Adams.*

WOLFE, H. R. I. & SCHOFIELD, A. L. **A Case of Filarial Funiculitis.** *Brit. J. Surgery.* 1946, Apr., v. 33, No. 132, 395–6, 3 figs.

An American Naval Air Gunner, aged 25, was stationed in tropical Africa from March, 1942, to May, 1944; he arrived back in America on February 10th, 1945, and was at once sent to hospital as a case of suspected strangulated

inguinal hernia. On the preceding day he felt a stab of pain in the left groin, which he thought was caused by the pressure of his parachute harness as he climbed down from an aeroplane to the flight deck of his ship.

On admission his temperature and pulse rate were normal; the left side of the scrotum was indurated and oedematous but the testicle and epididymis felt normal. The cord was thickened and tender up to the external abdominal ring. He had no other symptoms, and torsion of a testicular hydatid or acute funiculitis of unknown aetiology was diagnosed, and operation advised.

The cord and testicle were explored through a left inguinal incision; between the external abdominal ring and the testis the cord had expanded into a firm fusiform mass about the size of a walnut. On incising the tunica vaginalis the testis and epididymis appeared normal. The coverings of the cord were incised and examined. The vas deferens was inflamed and nodular and on its surface were some discrete yellowish nodules, 0·5–3 mm. in diameter, which on microscopic examination were seen to consist of lymphoid follicles packed with eosinophils, and they showed marked lymphangiectasis. The pampiniform plexus was engorged and some of its branches in contact with the inflamed vas were thrombosed. "An enormously dilated and varicose lymphatic was found running down to the upper pole of the testis. Through its thin wall the wriggling, white, hair-like coils of a worm were seen." It was excised and the worms were identified as *Wuchereria bancrofti*. Convalescence was uneventful and the patient left hospital three weeks after the operation. *J. F. Corson.*

CULBERTSON, J. T., ROSE, H. M. & OLIVER-GONZALEZ, J. **Chemotherapy of Filariasis due to** *Wuchereria bancrofti* **with Neostibosan.** *Amer. J. Hyg.* 1946, Mar., v. 43, No. 2, 145–51, 1 fig.

This paper describes the progress of an investigation, the earlier stages of which have already been reported [this *Bulletin*, 1946, v. 43, 54 & 354]. Briefly, 35 patients with microfilariae in the blood were given neostibosan. Twenty (Group I) were given 4·6 to 10·5 gm. in 33–54 days. Ten (Group II) were given the same course as Group I, but as this seemed relatively ineffective they were treated again 9 months later, with 5·9 to 12·5 gm. during 14 days. Five patients (Group III) were treated intensively, receiving 9·5–15·5 gm. in 13–14 days. The initial dose was 0·1 gm. injected intravenously; later this was worked up to two or three injections, each of 0·5 gm. per day.

Of the patients in Group I, 15 lost all their microfilariae in various periods up to 15 months after treatment, in three patients the microfilariae were greatly reduced in 15 months, and in two patients there was little change in 9 months. In the 10 patients of Group II who had resisted the first course, three lost their microfilariae in five months, in six the microfilariae were much reduced, and one showed only slight change. In Group III, two patients became microfilaria-negative in six months, and three lost at least half their microfilariae.

Among 15 control patients, none became microfilaria-negative in 14–17 months, and 11 showed considerable increase in the number of microfilariae present in the blood. Toxic reactions in the treated patients were relatively light, although half the patients experienced nausea and vomiting; two had severe nausea, anorexia and other symptoms, but it was not necessary to stop the drug in any patient. None of the treated patients has shown any sign of the development of elephantiasis, although such a hazard, as a result of treatment, has been suggested by some investigators. It is believed that neostibosan kills the adult worms, leaving the microfilariae to disappear slowly from the circulating blood because their number is no longer replenished.

F. Hawking.

PUIG SOLANES, M., FONTES, A. & ANTONIO QUIROZ, J. La onchocercosis en el estado de Chiapas. [**Onchocerciasis in the State of Chiapas, Mexico.**] Reprinted from *Rev. Salubridad y Asistencia.* 1945, July & Aug., No. 10, 30 pp., 19 figs.

This investigation into the ocular complications of onchocerciasis was carried out during February, 1945, under the auspices of the Pan-American Sanitary Bureau and the Mexican Health Department, in a part of the State of Chiapas where onchocerciasis was known to be endemic.

Ninety-three cases were examined, 92 of them proved by the presence of onchocerca nodules [elsewhere the number with nodules is given as 89], or by biopsy tests. One had superficial punctate keratitis, regarded as characteristic of the infestation, although no nodules were present. Of the 93, there were 64 males, 29 females; 76 were of mixed race, 13 were natives, 4 were not noted [but no mention is made of the relative constituents of these in the population, so that the racial incidence cannot be stated]. Fifty-two were under 20 years of age, and 16 below 10 years, 17 in the third decade [by ages, the total of cases amounts to 92; other discrepancies occur in the tables; for example, in one the cases over 10 years total 73, not 76]. Onchocerca dermatitis, present or past, was noted in 19 cases; biopsy was positive in 70 (79·5 per cent.), negative in 18 (20·4 per cent.) of 88 so tested.

The longest section of this contribution is devoted to the ocular symptoms present in this disease. Seventy of the 93 had demonstrable clinical signs; one had the embryos in the eye, but without clinical signs. In most of the patients eye symptoms appeared in 7–9 years after the earliest indications of infestation, and of the 70, 65 had nodules and 57 gave positive biopsy findings; microfilariae were found in the eyes of 29 patients. Sixteen presented the typical symptoms of burning, smarting and the sensation of the presence of a foreign body. Affection of the cornea was seen in 60, of the iris in 27; glaucoma secondary to onchocerciasis occurred in one. The commonest lesion of the cornea was a punctate superficial keratitis and refractile filiform opacities, usually bilateral and symmetrical. Some of the corneal deposits were the sites of dead microfilariae, and it may be that the death of the embryos was the real cause of the keratitis. This keratitis, strange to say, affected but slightly the acuity of vision. Of 61 examined, the vision was 10/10 in 45, 9/10 in 9. The iritis evolves very slowly, but seriously affects visual acuity. Of 18 with this complication, only two had normal vision, one had not even perception of light, and 14 others had vision 1/20 or less. Lesions of the fundus were very rare; the greater frequency in African patients is ascribed to the co-existence of other diseases, such as tuberculosis, syphilis, or trypanosomiasis. An additional reason must not be left out of account; patients in African records had had no treatment, whereas the majority of those studied in the present investigation had undergone periodical removal of nodules.

H. Harold Scott.

COHEN, H. H. **Trichinosis as a Cause of Meralgia Paraesthetica.** *J. Bone & Joint Surgery.* 1946, Jan., v. 28, No. 1, 153–6, 3 figs.

Meralgia paraesthetica is characterized by alteration of sensation, pain or diminished sensation, on the antero-lateral aspect of the thigh, on walking or by contact with clothing, and is ascribed to neuritis or to pressure on the external femoral cutaneous nerve. It has been found associated with pressure from a belt or corsets. The nerve runs close to the anterior superior iliac spine and passes over or under the sartorius, and pressure may thus be caused by an abnormally placed fibrous band.

The case here described is that of a man, 42 years of age, who had suffered for 4 years from numbness of this area, with " pins and needles " and hot and cold sensations. Walking increased the symptoms and often caused pain. Operation revealed that the nerve in question was being compressed by a dense fibrous band. Immediate relief was obtained by excision of this band. Section of the tissue removed revealed numerous cysts of *Trichinella spiralis*, but none of them calcified. A history was obtained of the patient having, a year before the onset of these symptoms, eaten pork and suffered after the meal from fever and diarrhoea. [There is no doubt of the association of the trichiniasis with the symptoms, but to what degree the parasite was aetiologically responsible is less certain. The fibrous band was present, but this may be so in the absence of any *Trichinella spiralis*.] *H. Harold Scott.*

AVERA, J. W., YOW, E. M., HARRELL, G. T. & FOWLER, Elizabeth B. **An Attempt by Feeding to induce in Animals Reactivity to *Trichinella spiralis* in the Absence of Infection.** *Amer. J. Trop. Med.* 1946, Jan., v. 26, No. 1, 125–31.

HARRELL and HORNE [*Bulletin of Hygiene*, 1945, v. 20, 469] found a significantly higher incidence of positive skin tests done with *Trichinella* antigen among patients in tuberculosis sanatoria and in hospitals for mental disease than among subjects in general hospitals. The length of stay in the institution seemed to be significant, but that study provided no evidence of the existence of unrecognized institutional epidemics of trichiniasis. THIBERGE (*J. Allergy*, 1944, v. 15, 298) reported that antigens contained in pollens can cross the mucosal barriers of the intestine and can cause symptoms in allergic subjects. If the sensitizing agent can cross the intact mucosa, ingestion of meat containing killed larvae of *Trichinella* might cause sensitivity. Cooking might denature the protein of *Trichinella*, but meat frozen to make it non-infective could be so incompletely cooked that the antigen might be unaltered. This might explain the high incidence of positive skin tests done on subjects in institutions. The present study was made to find out whether positive skin tests could be produced in animals not infested with *Trichinella*, by the ingestion of killed *Trichinella*. It showed that this did not happen and that the hypothesis just suggested did not explain the high incidence of positive skin tests in subjects in institutions. For details of the experiments the original should be consulted.

Discussing their results, the authors say that SPINDLER and CROSS (*Proc. Helminth. Soc. Wash.*, 1939, v. 6, 37) reported that skin sensitivity could be acquired by hogs by eating scraps of pork containing non-viable larvae of *Trichinella*, and that SCHWARTZ, in a personal communication, told them that hogs fed with cooked trichinized meat for several weeks gave weakly positive intracutaneous reactions to *Trichinella* antigen, although no trichinellae could be found in them. The present authors have been unable to reproduce this phenomenon in the guineapigs and rabbits which they used. The skin tests and flocculation tests recorded in this paper failed to show that animals fed with trichinized meat reacted to the antigens, nor did meat containing *Trichinella* larvae killed by freezing in order to avoid denaturation of the *Trichinella* protein produce positive skin or flocculation reactions. The present authors have not tried to find out whether the digestive juices of herbivorous animals can inactivate antigens of killed *Trichinella*, although THIBERGE (*loc. cit.*) states that ingested pollen is inactivated by the gastric digestion of man. The authors think that, because the degree of allergy in " trichinous individuals " is high, the passage of undenatured *Trichinella* antigen across the mucosa

might cause vague symptoms which might be attributed to allergy to pork but are really due to allergy to "the parasite contained in the meat." This "mechanism" might be responsible for the high incidence of *Brucella* skin tests, because antigen which has passed the mucosal barrier might produce sensitivity without infection.

Contrary to reports in the literature [see BACHMAN, this *Bulletin*, 1929, v. 26, 551] the authors were unable to produce strongly positive skin reactions to 1 : 200 dilutions of *Trichinella* antigen in guineapigs known to be infected. They consider that rabbits are better than guineapigs for skin and flocculation tests. The most clear-cut skin reactions were, however, obtained in the infected dog used and the authors suggest that rabbits, or preferably dogs, should be used rather than guineapigs for future skin tests. The authors cannot explain why the flocculation tests were not clearly positive in the infected guineapigs. No precipitin tests were done for comparison with them, but the flocculation test gave positive results in infected rabbits and detected an extremely mild degree of infection in one rabbit. The technique of this test is, however, "tricky" and needs large amounts of dried and powdered larvae. In its present stage of development it is probably not applicable to large-scale work, although it gives promise of being useful for the diagnosis of suspected cases. *G. Lapage.*

DESCHIENS, R. & COTTET, J. Étude expérimentale des acides et des sels biliaires dans l'oxyurose. [**Experimental Study of Bile Acids and Bile Salts in Enterobiasis.**] *Bull. Soc. Path. Exot.* 1945, v. 38, Nos. 11/12, 341–4.

DEFICIENCY DISEASES.

HUGHES, W. **Kwashiorkor and Ariboflavinosis.** *Trans. Roy. Soc. Trop. Med. & Hyg.* 1946, Apr., v. 39, No. 5, 437–48, 8 figs. on 4 pls. [16 refs.]

In Lagos three fairly well-defined syndromes of malnutrition may be distinguished—simple ariboflavinosis, kwashiorkor, and nutritional achromotrichia. These are not rigidly distinct ; simple ariboflavinosis, characterized by lesions of mouth, tongue and external genitals, is commonest among adults. Rare cases, however, occur in children, and these constitute a link between the adult syndrome and kwashiorkor. Achromotrichia appears to be a separate condition, in which muco-cutaneous lesions are minimal. It may be present in some cases of kwashiorkor, but alopecia is more common. It is suggested that nutritional achromotrichia may be caused by pantothenate deficiency.

The description that follows is based on the findings in 65 cases of kwashiorkor. Nearly half of these patients were two years old or less, although some cases were seen up to the age of 9 years. With increasing age the mortality and severity declined, and the condition merged into the simple ariboflavinosis of adults. It is argued that in kwashiorkor the epithelial lesions are essentially similar to those of adult ariboflavinosis, but more widespread, and more severe. The two conditions may perhaps be best contrasted in a table constructed from the author's data :—

	Adult Ariboflavinosis	*Kwashiorkor*
Mouth ...	Glossitis, cheilosis, angular stomatitis	Glossitis, cheilosis, angular stomatitis.
Face ...	Seborrhoeic lesions in naso-labial folds, at canthi, etc.	Fissures in naso-labial folds, at canthi, above ears.
Perineum ...	Dermatitis of scrotum ...	Scaling and exfoliation of prepuce, scrotum, vulva, and whole of perineum. Fissures and depigmentation.
Other parts ...	Typically, no change ...	Desquamation and exfoliation on extensor surfaces of limbs, dorsa of hands and feet, tips of nose and ears. Depigmentation and fissuring in flexures.

Many of the lesions listed above are illustrated by excellent photographs. Microscopically, the skin showed parakeratosis and acanthosis.

Other features of the disease were lethargy, anorexia, muscular wasting, bradycardia, anaemia, oedema, and signs of dehydration with oliguria. In four cases there was an abrupt and unexpected lapse into coma and death. At post-mortem examination the outstanding feature was fatty infiltration of the liver. The more the cases approached the typical, the more intense the fatty change.

The author points out that in experiments on riboflavin-deficient dogs SEBRELL [*Bulletin of Hygiene*, 1930, v. 5, 374] observed sudden death in coma, and a fatty liver post-mortem. These findings supported the view that kwashiorkor might be a result of ariboflavinosis. However, the results of treatment were disappointing; riboflavin in doses of 10 mg. parenterally rapidly cured the lesions of mouth and perineum, but it did not prevent death. Crude liver extracts seemed to produce some beneficial effect, particularly an improvement in appetite. In many cases death was precipitated by concomitant disease, such as malaria, tuberculosis, or septicaemia.

Summarizing, the author states that "it is something if we can recognize and follow the thread of riboflavin deficiency through the complicated pattern of kwashiorkor." "The severe case is probably suffering from many other deficiencies consequent on inanition." "Even if . . . the final hepatic lesion is the consequence of inanition, and quite beyond the influence of B_2-complex therapy, it will not alter the position from the preventive point of view." It is suggested that for prevention, attention should be concentrated on making available supplies of the B_2-complex, and that a practical source of this is food-yeast in a dosage of 10 grammes daily.

[In the treatment of kwashiorkor, nicotinic acid has been no more successful than riboflavin. Neither appears to have any effect on the liver lesion. The experimental evidence for the production of fatty liver by deficiency of B_2 vitamins, except choline, is slender. The liver lesion described by SEBRELL (*loc. cit.*) appears to be histologically different from that of kwashiorkor. On the other hand, there is much experimental evidence that a fatty liver can be produced by protein or amino-acid deficiency, and some clinical evidence that a high protein diet has a good effect on the liver in kwashiorkor. The recommendations made here for prevention must be examined in the light of this possibility—that the liver damage is not irreversible, and that it is the result of deficiency of protein or its derivatives. The recommended daily dose of 10 grammes of food yeast would supply 4 grammes of protein.]

J. C. Waterlow.

HUGHES, W. **Food Yeast in Tropical Malnutrition.** *Lancet.* 1946, Apr. 20, 569–72.

Feeding trials with food-yeast were carried out on prisoners and lunatics in Nigeria. In both these groups signs of riboflavin deficiency were very common,

being found in 25–30 per cent. of subjects examined. Four grammes of food yeast were given daily for five weeks to a group of 18 prisoners with severe signs of deficiency. At the end of this time, the number with lesions was reduced to five, of whom only one was severely affected. During the following three weeks, when no yeast was given, six patients relapsed. In a control group of untreated prisoners, there was no change in the incidence of severity of the lesions.

In a second experiment, 145 male lunatics received 8 gm. of food-yeast daily for seven weeks. The number of cases with signs of riboflavin deficiency fell from 45 to 18, and the severity of the lesions decreased. In a control group of female lunatics who did not get yeast, there was no change in the incidence of lesions, and the severity increased. In a similar trial on prisoners, 9 gm. of yeast were given daily for eight weeks. Out of 64 cases with signs of riboflavin deficiency, 56 were cured.

It is concluded that 10 grammes of food-yeast daily would be enough to prevent manifestations of riboflavin deficiency in the population of Lagos. This amount of food-yeast contains about 0·5 mgm. of riboflavin.

[No estimate is given of the riboflavin content of the average Nigerian diet, so that it is not possible to see how far the recommended supplement of 0·5 mgm. goes towards filling the gap between actual intake and optimum requirement. Adequate nutrition is not necessarily achieved with the correction or prevention of clinical deficiency.] *J. C. Waterlow.*

SPIES, T. D. & MOREY, Mabel M. **A Clinical Study on the Use of a Protein Supplement in treating Persons with Nutritive Failure.** *Southern Med. J.* 1946, Feb., v. 39, No. 2, 117–21, 5 figs.

In the last few years it has gradually though rather tardily been recognized that in the clinical conditions we call deficiency diseases, the deficiency is one of several nutrient factors and that these include not only the so-called vitamins —in other words the term deficiency disease is not synonymous with hypo-vitaminosis. The authors say "we are becoming increasingly aware of the extent of the protein deficiency in many diets and its role in nutritive failure. . . . We are studying not only the effect of individual amino acid on persons with deficiency diseases but also the effect of complex concentrated proteins such as hydrolyzed casein."

The case histories of two patients, selected from a group of 16 with pellagra, anaemia and oedema are given to illustrate the effect of the latter.

The administration of hydrolysates appeared to clear up the oedema and in some cases the cheilosis, which had proved resistant to riboflavin.

Apart from the attempt to show experimentally the specific effect of protein hydrolysates on certain symptoms, it would appear that these have no advantage over a correct diet containing meat, milk and eggs. *H. S. Stannus.*

GOPALAN, C. **The "Burning-Feet" Syndrome.** *Indian Med. Gaz.* 1946, Jan., v. 81, No. 1, 22–6.

The author gives an excellent description of the syndrome "burning feet" —"Kal erichal," in Tamil—well known to medical men who have had opportunities for making observations among indigenous populations during the past half century. He quite correctly states that the condition should be clearly distinguished from peripheral neuritis and beriberi, with which it has often been confused by authors whose observations have not been made with sufficient care.

This article is based on 53 cases, 14 males and 39 females, from among a poor population living on a parboiled rice gruel and cheap vegetables. Among the women 27 gave a history of parturition within a few weeks of being seen.

In practically all the patients, signs of riboflavin deficiency were present—glossitis, angular stomatitis, angular blepharitis; in some superficial keratitis was present, in a fair proportion of the males scrotal dermatitis was noted and in the women leucorrhoea was present [no slit-lamp examinations, apparently, were made].

The burning pain commonly began in the region of the ball of the big toe, then spread over the sole, and sometimes involved the dorsum of the foot and ankle; less often the palms of the hands were involved.

Some cases were seen in which excruciating paroxysms of burning pain alternated with freedom from it.

Associated with this symptom, sensations of pins and needles were complained of, as noted by other observers, but the two did not necessarily parallel each other.

Hyperidrosis, another well-known symptom of the syndrome, was noted as occurring in the areas of burning pain. On the other hand there was no muscular wasting or tenderness, no loss of power, no paralysis, no spasticity, no loss of reflexes, no sensory loss of any kind.

There was no response to thiamin or nicotinic acid; treatment with riboflavin, while clearing up the signs of hyporiboflavinosis, left unchanged the burning pain syndrome; rapid improvement and cure, however, followed upon the daily intramuscular injection of 20 to 40 mgm. calcium pantothenate for 2–3 weeks, in 10 cases submitted to the treatment.

In discussing the pathology [pathogeny] of the condition reference is made to the abridged version of the Lumleian Lectures for 1944 [this *Bulletin*, 1944, v. 41, 862] in the following words: "Stannus (1944) has, indeed, suggested that 'burning feet' is part of the syndrome of ariboflavinosis." [This is of course incorrect, as throughout those lectures—entitled Some Problems in Riboflavin and Allied Deficiencies—it was made clear that the syndromes described were due to a hyporiboflavinosis alone or associated with a deficiency of another closely allied factor of the B complex.] In further discussion no fresh data are supplied and no definite conclusions are reached in regard to pathogeny. *H. S. Stannus.*

SPRUE.

Spies, T. D., Milanes, F., Menéndez, A., Koch, Mary B. & Minnich, Virginia. **Observations on the Treatment of Tropical Sprue with Folic Acid.** *J. Lab. & Clin. Med.* 1946, Feb., v. 31, No. 2, 227–41, 4 figs.

Nine patients suffering from tropical sprue were treated, under standardized conditions, with folic acid by mouth in dosage ranging from 10 to 200 mgm. daily. The response of those receiving only 10 mgm. closely paralleled that of those receiving higher doses, and was manifest by a rapid improvement in each patient's feeling of well-being, an increase in appetite, a gain in weight and strength, a decrease in the pigmentation of the skin, together with resolution of the glossitis, soreness of the mouth and burning of the rectum. This clinical improvement was accompanied by a striking haematological improvement. In all cases a maximal reticulocytosis occurred, the day of the peak ranging from the sixth to the ninth day, which was followed by rises in the red cell count varying from 0·50 to 1·21 million per cubic millimeter in 14 days in the patients receiving 200 gm. folic acid, and from 0·46 to 0·71 million in those

receiving 10 mgm. doses. The haemoglobin levels of all the patients increased as the erythrocyte counts increased, while the leucopenia generally accompanying the macrocytic anaemia decreased. Normal control subjects receiving 200 mgm. folic acid orally for ten days showed no changes in their erythrocyte counts, haemoglobin levels, leucocyte counts or in the number of reticulocytes in the four weeks following the administration of the drug. The bone marrow of the patients with sprue treated with folic acid, showed macroscopically a gross change from light red, thick, gelatinous marrow to deep red fluid containing discrete clumps of cells, and microscopically the erythroblastic arrest of the disease was replaced by a normoblastic hyperplastic regeneration, with a shift in the ratio of white cells to nucleated red cells from 5 : 2 to 5 : 6.

The paraesthesiae of the hands and feet were not markedly affected by the administration of folic acid, but the oedema disappeared in all but two patients. The diarrhoea followed a variable course, gradually decreasing in most cases, although in some the faeces failed to improve, while in others initial improvement would sometimes be followed by reversion for a day or so to copious, frothy stools. [See also SPIES, below.] *F. Murgatroyd.*

DARBY, W. J., JONES, E. & JOHNSON, H. C. **Effect of Synthetic Lactobacillus Casei Factor in Treatment of Sprue.** *J. Amer. Med. Ass.* 1946, Mar. 23, v. 130, No. 12, 780–86, 7 figs. [Refs. in footnotes.]

A deficiency syndrome in the monkey, characterized by anaemia, leucopenia, diarrhoea, oral lesions, facial oedema, loss of weight and death, can be prevented by a factor, sometimes referred to as vitamin M, which has been differentiated from nicotinic acid, riboflavin, thiamin, panthothenic acid, choline, *para*-aminobenzoic acid, pyridoxine and inositol. Certain purified liver extracts which were effective in the treatment of pernicious anaemia also failed to prevent the nutritional cytopenia in the monkey. Monkeys deficient in vitamin M respond, however, to the intramuscular administration of small quantities of a highly purified *Lactobacillus casei* factor, and the various similarities of vitamin deficiency in the monkey to the sprue syndrome in man led to a test of the efficacy of the newly synthesized *L. casei* factor in the treatment of three patients suffering from sprue.

The patients were maintained on standardized diets devoid of organ meats, and the crystalline *L. casei* factor was given intramuscularly in a dosage of 15 mgm. daily. The response of the patients resembled that following the administration of an active liver preparation. Within two or three days all the patients experienced a feeling of improvement, the glossitis was relieved by the fourth or fifth day, and simultaneously there was a cessation of the diarrhoea and an increase in appetite. A gain in weight commenced on approximately the fifth to the seventh day, the initial gain apparently reflecting water retention, as it was accompanied by demonstrable oedema and haemodilution which disappeared about the twelth to the fourteenth day ; subsidence of this oedema was followed by a striking increase in weight unaccompanied by water retention.

Although the diarrhoea was promptly relieved, stool analyses did not show a return to the normal fat content, while, furthermore, the patients did not exhibit an increase in plasma carotene, a finding also consistent with the continued presence of an excess of fat within the gastrointestinal lumen.

The treatment brought about increases in all the formed elements of the blood ; and the bone marrow, which prior to treatment showed a megaloblastic arrest, returned to normal ten days after treatment was begun.

The evidence suggests that the administration of this *L. casei* factor will result in a satisfactory response in cases of sprue, pernicious anaemia, macrocytic anaemia of pregnancy and nutritional macrocytic anaemia. Unpublished data

indicate that the factor is effective only in those macrocytic anaemias with hyperplastic primitive marrow, so-called dysplastic and aplastic anemias failing to respond, even though examination of the peripheral blood indicated a macrocytic anaemia.

From the relationship outlined, the authors suggest that vitamin M deficiency in the monkey is the experimental analogue of sprue in man. As the term folic acid has been so loosely used, they feel that its retention can but lead to confusion, and they propose that the group of substances which possess similar haematopoietic activity for primates be referred to as the vitamin M group [see SPIES, this *Bulletin*, 1946, v. 43, 582; SPIES *et al.*, above].

The doses given to the patients in these experiments are probably in excess of the minimal amount which would produce a maximal response. A reticulocyte response has been reported in two patients suffering from pernicious anaemia who were given intravenously only 2 mgm. daily, and from a comparison of the requirements of chicks for riboflavin and the *L. casei* factor, it is suggested that in man the maintenance dose of the *L. casei* factor may be of the order of 0·1 to 0·2 mgm. daily and that the curative dose may be about 1 mgm. daily. No local or systemic toxic effects were, however, observed from the administration of the material, in the doses employed, to 12 persons manifesting a variety of blood dyscrasias. [See also this *Bulletin*, 1946, v. 43, 667.] *F. Murgatroyd.*

HAEMATOLOGY.

SPIES, T. D. **Effect of Folic Acid on Persons with Macrocytic Anemia in Relapse.** *J. Amer. Med. Ass.* 1946, Feb. 23, v. 130, No. 8, 474–7.

Folic acid was given parenterally or orally in amounts of 20 mgm. or more daily to 45 patients suffering from anaemia, including 8 patients with nutritional macrocytic anaemia, 8 with pernicious anaemia, 11 with sprue, 3 with anaemia associated with pregnancy, 1 with anaemia, associated with carcinoma, 1 with anaemia associated with chronic alcoholic addiction, cirrhosis of the liver and neuritis, 3 with anaemia of undetermined origin, 3 with aplastic anaemia, 3 with anaemia associated with leukaemia, and 4 with iron deficiency anaemia. None of the patients with aplastic anaemia, iron deficiency anaemia, or the anaemia associated with leukaemia showed any improvement, but there was a very marked subjective and objective improvement following the administration of folic acid to those suffering from macrocytic anaemias. These latter patients experienced an immediate feeling of improvement, together with an increase in strength, vigour and appetite. This subjective improvement coincided with, or was followed by, an increase in the reticulocytes of the peripheral blood, and by subsequent rises in the red blood cell counts and in the haemoglobin content of the blood. This improvement occurred regardless of the mode of administration of the drug. The minimal and optimal doses of folic acid have not yet been determined, and there appears to be some variation from patient to patient. It has been found, however, that while 400 mgm. daily may be administered without untoward symptoms, as little as 5 to 10 mgm. parenterally or 10 mgm. orally each day will often produce a maximal haematopoietic response. It has also been found that patients failing to respond fully to 3 to 4 mgm. folic acid daily may respond to liver extract or yeast administered in amounts which supply only 1 mgm. or less of folic acid daily, which suggests that the antianaemic factor present in liver extract or yeast may be a combination of chemical substances. *F. Murgatroyd.*

SPIES, T. D., VILTER, C. F., CLINE, J. K. & FROMMEYER, W. B. **The Substitution of Thymine for Folic Acid in the Treatment of Macrocytic Anaemias in Relapse.** *Southern Med. J.* 1946, Mar., v. 39, No. 3, 269–70. [12 refs.]

It has been shown that thymine (2, 4-dihydroxy-5-methyl-pyrimidine), an integral portion of cells, and occurring as part of nucleic acid, could replace folic acid as a growth factor for lactic acid bacteria provided that other essential substances, including adenine, guanine, or xanthine, were present, but the amount of thymine required was 5,000 times as great as that of folic acid. It was suggested that folic acid acts as an enzyme or coenzyme in the synthesis of thymine or a thymine-like compound, which is used by the bacteria to form nucleic acid.

If this represents a fundamental biochemical mechanism of cellular activity, it is possible that thymine might replace folic acid in the maturation of the cellular elements of the blood, and the amount of thymine required might be of the order of 12·5 to 25 gm. daily, since some patients with macrocytic anaemia respond to as little as 2·5 to 5 mgm. of folic acid daily.

Six patients with nutritional macrocytic anaemia and the anaemia of sprue showed no response to thymine in doses of 5 to 50 mgm. daily for ten days. One patient given 500 mgm. twice daily for six days also showed no response, but when the dose was increased to 2 gm. thrice daily for 14 days a reticulocytosis of 14·2 per cent. was reached on the eleventh day, and concomitant with this response there was a subjective improvement, and appreciable decrease in the symptoms referable to the glossitis. The erythrocytes also rose from 2·01 million to 2·74 million and the haemoglobin from 6·3 gm. to 9·4 gm. on the twentieth day of the treatment with the large dosage. Thereafter, without further treatment, the reticulocytes subsided but the erythrocytes increased to 2·88 million and the haemoglobin to 10·4 gm., while the bone marrow reverted from a condition of megaloblastic arrest to normal.

F. Murgatroyd.

COOPERMAN, J. M., ELVEHJEM, C. A., MCCALL, K. B. & RUEGAMER, W. R. **"Folic Acid" Active Compounds in the Nutrition of the Monkey.** *Proc. Soc. Exper. Biol. & Med.* 1946, Jan., v. 61, No. 1, 92–7, 2 figs. [13 refs.]

A norite eluate concentrate, extractable from yeast or from liver extract, appears to contain at least three factors, namely, folic acid necessary for the growth of *Lactobacillus casei*, vitamin B_{10} necessary for normal feathering in chicks, and vitamin B_{11} necessary for normal growth in chicks. A crystalline compound which has properties similar to those of this concentrate, and which has been called vitamin B_c, can be isolated from liver, while a vitamin B_c conjugate has been isolated from yeast and is active for the chick but has no activity for the bacterium. Upon enzymic digestion, however, this B_c conjugate becomes active as a source of B_c for *L. casei.*

A deficiency of folic acid in monkeys leads to a syndrome, a prominent feature of which is leucopenia; and experiments showed that crystalline B_c and a synthetic *L. casei* factor were active in doses of 100γ daily, that the B_c conjugate was less active in doses of 200γ and 300γ daily, and that B_{10} and B_{11} concentrates were inactive as sources of folic acid. The folic acid deficiency also precipitates a deficiency for the monkey anti-anaemic factor which is characterized by lack of growth, a suboptimal haemoglobin level, and a reversal in the neutrophile-lymphocyte ratio. While B_c conjugate, B_c, and the synthetic *L. casei* factor were effective in raising the leucocyte count, the addition of whole liver was necessary to correct the neutrophile-lymphocyte ratio, the low haemoglobin level, and the loss in weight. *F. Murgatroyd.*

GIBSON, Q. H. & HARRISON, D. C. **An Artificial Standard for Use in the Estimation of Haemoglobin.** *Biochem. J.* 1945, v. 39, No. 5, 490–97. [15 refs.]

A satisfactory standard for general use in haemoglobinometry should be reproducible, stable, easily prepared, and have an absorption spectrum closely similar to that of the blood derivative with which it is to be compared. These requirements appear to be fulfilled by a standard solution of a mixture of organic salts prepared according to the following directions :—Weigh out 11·61 gm. of $CrK(SO_4)_2 \cdot 12\ H_2O$ (Analar), using crystals free from any sign of whitening due to efflorescence, 13·10 gm. of anhydrous $CoSO_4$, or the equivalent weight of the hydrated salt, and 0·69 gm. of $K_2Cr_2O_7$; dissolve in about 500 ml. of distilled water, add 1·8 ml. of N-H_2SO_4, and heat to boiling. Boil for 1 minute, cool well and make up to 1,000 ml. with distilled water. A more precise method of preparing the standard is also described, but solutions prepared by the simplified method given above, show readings in the absorptiometer in close agreement with those shown by the precise standard. The standard should be stored in a glass-stoppered bottle free from grease and organic material, and ethanol or acetone should not be used for drying apparatus used to contain the standard.

For the routine determination of blood haemoglobin, pipette 10 ml. of a clear solution of 0·1 N-NaOH into a dry boiling tube fitted with a loosely fitting ground-glass stopper ; ordinary corks must not be used as they give a colour with the alkali. Pure NaOH (Analar) should be used, as some impure samples of NaOH give an opalescence when heated with blood, and the solution should be stored in a Pyrex vessel. Add 0·1 ml. of blood, stopper and mix gently for a few minutes until the solution is clear. Take about the same volume of standard in a similar tube and immerse the two tubes with the stoppers loosened in a vigorously boiling water-bath, so that the solutions in the tubes are just below the level of the water. Heat for exactly 4 minutes, after which at once cool thoroughly by immersion in cold water and mix by inversion. The haemoglobin can then be determined by visual comparison of the two solutions in a colorimeter, preferably with a green filter over the eyepiece, the haemoglobin value of the standard being taken as 16·0 gm./100 ml. using filters, and 16·2 gm./100 ml. using unfiltered light. With standardized light and filters the determinations may be made with a photometer or a photoelectric absorptiometer.

The systematic error involved in using the standard as described should not exceed $\pm 1{\cdot}5$ per cent., *i.e.* $\pm$ 0·2 gm. of haemoglobin/100 ml. in a normal blood, and in view of the variability of blood samples from the same individual, it would appear that no practical advantage would be gained from a greater degree of precision.

During determinations of haemoglobin by various methods, a consistent difference was found between the values calculated from Fe determinations and oxygen capacity measurements of normal blood. The difference was not due to the presence of carboxyhaemoglobin or methaemoglobin, nor due to neglect of plasma iron, but indicated the presence of some 3 per cent. of iron in a non-functional form in normal blood. *F. Murgatroyd.*

DEWHURST, K. E. **The "Cooke-Ponder" Lobular Neutrophil Count on the East African Askari.** *East African Med. J.* 1946, Feb., v. 23, No. 2, 47–50.

The usual procedure for classifying the neutrophil leucocytes into their different maturity groups consists of determining the various percentages of

the cells having one, two, three, four, and more than four lobulated nuclei, as shown in 100 consecutive cells of a thin film stained by Giemsa's method. The criterion of separate lobulation is that either the lobes appear detached or are joined only by a thin filament of chromatin ; if there is any doubt about the number of nuclear lobes the cell should be classified in the lower class. Various indices are used to express the results of such a count, the commonest being the Arneth Index, which is obtained by adding the percentages of cells in the first, second and one-half of the third class. Another method of expression is by the weighted mean of the percentage counts, a figure obtained by multiplying the number of cells in class I by 1, the number in class II by 2, and so on to class V, the sum of the figures so obtained being then divided by the total cells counted, namely 100. A higher Arneth Index than 58·5 or a lower weighted mean than 2·75 is taken to indicate a " shift to the left " from the normal for Europeans ; such shifts have been found in routine surveys of bloods from Egypt, Malaya and China.

The present paper records the results of a survey of 500 apparently healthy indigenous East Africans, drawn from the following tribes, Jaluo, Kikuyu, Baganda and Munyamwezi. No significant tribal differences were noticed, and for the total survey the results were :—neutrophils of class I, 14 per cent., class II, 41 per cent., class III, 36 per cent., class IV, 8 per cent., and class V, 1 per cent., giving an Arneth Index of 73 and a weighted mean of 2·4. If no " shift to the left " be claimed until the Arneth Index exceeds the extreme limit of the European index of 65, which gives a truer comparison than that obtained from the European mean of 58, the following results were found :—18 per cent. of the Africans had no shift to the left (Arneth Index below 65), 17 per cent. had a very slight shift (A.I. 65–70), 40 per cent. had a moderate shift (A.I. 70–80), and 25 per cent. had a marked shift (A.I. over 80). The shift to the left in the Africans was chiefly due to a marked increase in the cells of class II, namely the newly segmented neutrophils of the peripheral blood. *F. Murgatroyd.*

BEET, E. A. **Sickle Cell Disease in the Balovale District of Northern Rhodesia.** *East African Med. J.* 1946, Mar., v. 23, No. 3, 75–86, 1 map.

Using vaseline-sealed cover-glass preparations of capillary blood examined at intervals up to 48 hours, the author found that the overall incidence of the sickle cell trait in 815 consecutive in-patients of the Government Hospital at Balovale, an isolated rural area of Northern Rhodesia, was 12·9 per cent., the incidence among males being 12·5 per cent. and among females 13·3 per cent. The incidence of the condition among children, that is among those under approximately five years of age, was 17·6 per cent., whereas for those above this age the incidence was only 12·1 per cent. A few patients were examined for sickling *in vivo*, but the condition was not so demonstrated. Some were also examined for the trait by the method of sealing citrated blood under paraffin in test-tubes, with fixation of the cells by the addition of formalin at the end of 48 hours ; to obtain the best results it was found that the citrate solution should be boiled before use in order to expel all air.

It was difficult to assess the amount of anaemia due to sickle cell disease, as 48·7 per cent. of the population harboured hookworms, 22 per cent. *S. haematobium*, 2·5 per cent. *S. mansoni*, while in addition, at the height of the rains in February, 92 per cent. of the children under five years of age had malaria parasites. The incidence of helminthiasis was the same among patients with or without the sickle cell trait, but it was found that when the transmission of malaria was at its lowest the parasite rate for sicklers was considerably less

than for the non-sicklers, whereas the rates were approximately equal for sicklers and non-sicklers at the height of the rains when malaria was most prevalent.

The familial character of the sickling cell phenomenon was confirmed, as the incidence of the trait among the offspring of a group of 33 affected parents was 65 per cent., but there was no evidence that the trait was sex-linked.

The Balovale District can be divided into seven areas, and study of the incidence of the sickle cell trait in these and adjacent areas suggests that there have been little, if any, movements of populations within the District from east to west during recent years, that there has been considerable emigration of Portuguese natives into the land east of the Zambesi River but little into the land west of the River, and that the amount of emigration of Northern Rhodesian Lovale, resident west of the River, over to the east bank has been small compared with that from the north by the Portuguese Lovale into the same part of the District. This last conclusion is unexpected, although the others are more or less borne out by what is known of the history of the District. No detailed investigation of the origin of the Lovale now residing east of the Zambesi has ever been made, however, and in view of the haematological findings it is suggested that an investigation of this nature should be undertaken, since definite information on the point would have administrative value.

F. Murgatroyd.

VENOMS AND ANTIVENENES.

SOBRINHO, O. P. Anaveneno e o seu valor na produção de soros anti-ofídicos. [**Anavenene for preparing Antisera against Snake Venoms.**] *Arquivos do Inst. Químico-Biol. Estado e Minas Gerais.* 1945, v. 1, 27–32. English summary (5 lines).

In 1936 the method of production of antivenenes was to prepare a stock venene consisting of venom 10 gm., glycerin 80 cc., normal saline 120 cc. For stock *Bothrops* venom a mixture was made of *B. jararaca* 6 gm., and 1 gm. of each of *B. alternata*, *B. beuweidii*, *B. atrox* and *B. jararacussu*, in 0·75 per cent. saline, and fragments of camphor were added to preserve it. This was left at room temperature for a month, with daily shaking. It was then injected subcutaneously, twice weekly, into horses, starting with a dose of 0·075 mgm. and by the 25th injection the dose had reached 350 mgm.; the total period of immunization was about three months. To obtain a more potent serum, 13 more injections were made, till at the 38th a dose of 1,000 mgm. was injected.

Another method has more recently been put into operation, *viz.*, the use of anavenene. For preparing this, 13·33 gm. of the venom are triturated with 333·33 cc. glycerin, 13·33 cc. formol, and saline to make a litre; the mixture is placed in a thermostat at 37°C. for 40 days and then filtered. Horses were inoculated subcutaneously with this, 42 injections in 245 days, starting with 0·005 mgm. and increasing gradually to 0·450 mgm. The first 14 injections were given every four days, after that once a week. The serum so obtained was very satisfactory "neutralizing 1·5 mgm. of the venom" [per cc. ?]. Later still using a preparation containing 10 gm. of venom, 330 cc. glycerin and 10 cc. formol, the period of immunization was reduced by eight weeks. One great drawback to this method is the frequency with which abscesses follow inoculations, but these are in most instances sterile, which is not the case when venom itself is used.

H. Harold Scott.

MARTINS, A. V. Sôbre o uso do anaveneno na produção do sôro anti-escorpiônico. [**Anavenene in the Production of Scorpion Antivenene.**] *Arquivos do Inst. Quimico-Biol. Estado de Minas Gerais.* 1945, v. 1, 7–18. [10 refs.] English summary.

MAGALÄES in 1908 prepared a serum against scorpion venom by injecting intravenously into oxen increasing doses of scorpion venom and using camondongos as his test animals. The author has modified this method in each particular: He uses the horse instead of the ox, the anavenene in place of the venom, subcutaneous inoculation in place of intravenous, and guineapigs instead of camondongos. His objections to the ox are: that the amount of serum obtained is less than that from the horse, that ox-serum is relatively toxic to some laboratory animals and to man, that there is a risk of anaphylaxis to those sensitized to beef protein, and, lastly, the horse is a more docile animal for these injections. The use of anavenene is preferable to venom because its toxicity is much reduced while its antigenic potency is retained. Guineapigs are easier to rear and to maintain than are camondongos.

The horses were inoculated every 6–7 days with increasing doses of the anavenene of *Tityus serrulatus*, and tests were made after the 8th–9th injections; others after the 7th and 15th.

The author claims, and his protocols support the claim, that by his method he obtains much larger amounts of antivenene, which, moreover, has greater antitoxic potency and is produced in less time than by the older mode of procedure. *H. Harold Scott.*

MARTINS, A. V. Anaveneno escorpiônico. [**Scorpion Anavenene.**] *Arquivos do Inst. Quimico-Biol. Estado de Minas Gerais.* 1945, v. 1, 19–26. English summary (5 lines).

The preparation of scorpion antivenene by repeated injection of the venom into animals has several drawbacks; the author, consequently, tried using the anatoxin (anavenene) to determine whether it would prove as useful in preparing scorpion antivenene as the corresponding product had proved serviceable for snake antivenenes. He found that by addition of toluol in gradual quantities to form a layer some 5 mm. thick over the venom contained in dark-coloured vials and kept at 4°C., the venom could be preserved for several months without loss of toxicity. If kept at 37°C. its toxicity was reduced to one-sixth in six weeks.

He next found that addition of 1 per cent. formol to the venom and maintaining the mixture at 4°C. reduced the toxicity to about one-tenth without affecting its antigenicity. *H. Harold Scott.*

DERMATOLOGY AND FUNGUS DISEASES.

GOLDBERG, L. C. **An Unusual Lichenoid Dermatosis.** *J. Amer. Med. Ass.* 1946, Mar. 23, v. 130, No. 12, 775–80, 10 figs.

This is another report concerning the lichen planus-eczematoid dermatitis complex which has been described on several occasions in American literature, and which has received attention in the British medical press [see this *Bulletin*, 1946, v. 43, 149; 301; 479].

Except in regard to therapy, Goldberg has little new information to add. His observations are based upon a large number of patients returned, because

of this malady, to the United States from the South Pacific Theatre of Operations and geographically similar areas. Like other authors, he describes phases of dermatitis, exfoliative dermatitis and lichenoid eruptions, which may occur during the course of the disease. He states that he has never seen a classical lichen planus papule with Wickham's striae in an original case, although such lesions have been seen in three relapsing cases. The typical lesion of the lichenoid phase is similar to that occurring in hypertrophic lichen planus, rather than to the polygonal, umbilicated papulo-squamous lesion described by Erasmus WILSON. Goldberg records that the lichenoid papules are often present on the face, especially the eyelids and ears, and he describes an appearance similar to erythema ab igne which may be noted on the eyelids when the eruption subsides. In 12 out of 60 cases studied, the mucosae of the mouth, lips, penis or vulva were involved ; and in 3 out of 20 patients examined proctoscopically, greyish white mucosal alteration was seen in the rectum on the columns of Morgagni, the crypts not being involved. Gastroscopy failed to reveal lesions on the gastric mucosa. In a discussion of the aetiology, Goldberg states that he has been unable to reproduce the lesions by the administration of atabrine [mepacrine] in the cases observed. "All these [patients] were maintained on suppressive atabrine therapy while they were being treated and in no instance did any new lesions appear while under observation. It is true, however, that some of the hypertrophic lesions would weep, but this could readily have been a reaction to local treatment. . . . Several patients developed their first attacks of malaria or relapsed while in this hospital, and were treated with intensive atabrine therapy, but there was no aggravation of their skin lesions. One patient in particular, with severe exfoliating dermatitis plus his lichenoid lesions, has been observed for eight months, during which time he has been receiving continuous suppressive atabrine therapy ; he has recovered except for scattered sepia brown pigmentation. Patch and intradermal tests with atabrine were done in a few of these patients and all were found to be negative. No passive transfer tests were made." "Although atabrine may be a definite causal factor or an agent that prepares the soil, more evidence will have to be uncovered before it can be pinned down as the exclusive and certain etiologic factor." Goldberg suggests that "the neurophysiovascular mechanism, photosensitivity and infection appear to play roles, as may as yet unknown geographic factors." He could not reach any definite conclusions "as to a possible nutritional factor in producing this dermatosis."

In the treatment of the dermatitis phase the mildest salves and lotions could be used, for the skin was easily irritated. Exfoliating cases were treated by the usual methods employed in any exfoliating dermatitis, such as continuous wet dressing with 1/5000 potassium permanganate solution, corn starch and baking soda baths, high caloric diets, with added vitamin medication, and the intramuscular administration of crude liver extracts in doses of 2 to 5 cc. every day, or on alternate days ; "amino acids were given orally in large amounts." In the lichenoid phase, small doses of oxophenarsine hydrochloride ["Mapharsen"] were given, 0·02 gm. bi-weekly ; many of the patients responded well, and the pruritus was often relieved before the third injection. The lesions of the mucosae responded equally with those on the skin. In no case were more than ten injections required to cause involution of the lesions. Several of the patients treated with "Mapharsen" developed fever up to 102°F. about six hours after the first injection, and, when this happened, administration of the drug was discontinued. It was believed that these cases had a "subthreshold hepatitis" which might have been caused by atabrine and activated by the arsenical injection, for their icterus indices were raised and some developed clinical jaundice. The reactions subsided in 48–72 hours,

during which time the patients suffered from nausea and vomiting which could be relieved by intravenous injection of a litre of 10 per cent. glucose solution and the oral administration of amino acids.

The author notes that before admission to his hospital, many of the patients had received penicillin in large amounts, both intramuscularly and locally, but no benefit accrued except that secondary infection was controlled. "Many also had received sulfonamides, both internally and locally, with no real gain and even with occasional harm." *R. M. B. MacKenna.*

WEIDMAN F. D. & KLIGMAN, A. M. **A New Species of Cephalosporium in Madura Foot** (*Cephalosporium granulomatis*). *J. Bacteriology.* 1945, Nov., v. 50, No. 5, 491–5, 3 figs.

TWINING, DIXON & WEIDMAN [this *Bulletin*, 1946, v. 43, 674] reported a case of mycetoma caused by a new species of *Cephalosporium* which is described in the present paper under the name *Cephalosporium granulomatis* n. sp. Weidman & Kligman. It presents the following morphological characters: "Hyphae slender, 0·5 to 1·5μ, hyaline, sparingly septate. Conidiophores erect, nonseptate, unbranched, slightly tapering towards the tip, 14 to 28$\times$ 0·5 to 1·5μ. Spore heads globose, 5 to 11μ, containing 6 to 24 conidia; heads at first with conspicuous gelatinous capsule rupturing abruptly to discharge the conidia which remain embedded in a gelatinous matrix. Conidia at first mostly rod-shaped with blunt rounded ends or oblong elliptical. Later, the conidia may show a diversity of shapes, becoming variously ovoid, elliptical or obovate; 2·8 to 3·5$\times$0·7 to 1·3μ. Young conidia frequently with refractile globule at both poles. Coremia readily formed in all media; germination of conidia uni- or bi-polar. Chlamydospores formed in blood media at 37°C. but not in the usual media at room temperature."

Descriptions are given of the appearances of cultures of the fungus on various media and the paper is completed by the diagnosis of the new species in Latin. *J. T. Duncan.*

CHERRY, C. B. & BARTLETT, A. G. **The Diagnosis of Acute** *Coccidioides immitis* **Infections.** *Bull. U.S. Army Med. Dept.* 1946, Feb., v. 5, No. 2, 190–93.

The diagnosis of coccidioidomycosis is at times difficult, and the authors issue a timely warning against the acceptance of the coccidioidin skin reaction as a diagnostic test of active disease, if unsupported by more trustworthy evidence, for persons who have lived in the endemic areas of coccidioidomycosis may present a high degree of skin sensitivity to coccidioidin for many years afterwards, in the absence of infection. The clinical signs of a pulmonary disorder with febrile symptoms, an initial leucocytosis and an eruption of erythema nodosum or multiforme, supported by a radiological picture of infiltration of the lung and hilar adenopathy, are not more than suggestive, even when associated with a history of recent exposure to the disease. Valuable confirmatory evidence is furnished by positive serum complement fixation and precipitation reactions with *C. immitis* antigen. Both of these reactions are given in the early stages of the disease, but the precipitation reaction tends to diminish and disappear fairly soon, while complement fixation may be obtained for months or even years. The best diagnostic evidence is the presence of *C. immitis* in the sputum, proved by culture or by inoculation into guineapigs. Direct microscopical examination of the sputum is not a trustworthy test and it usually fails to reveal the parasite.

Just as a positive coccidioidin skin reaction need not imply active disease unless the patient's history indicates *only* very recent exposure to infection,

so a negative result to the test may not exclude the infection in (1), a very recent infection in which skin sensitivity has not yet developed, and in (2), a severe generalized infection with a condition of anergy. Except for these two conditions, a negative result may be taken to exclude infection if the test has been properly conducted.

Coincident tuberculosis complicates the diagnosis, for both diseases may present a similar symptomatology and radiological picture, and if the coccidioidin and tuberculin tests are both positive, repeated search for the causative fungus offers the only hope in diagnosis. *J. T. Duncan.*

GOREN, M. L. **Localized Coccidioidomycosis of Bone. Report of a Case.** *J. Bone & Joint Surgery.* 1946, Jan., v. 28, No. 1, 157–60, 2 figs.

In coccidioidomycosis the common portal of infection is the lung, through inhalation of dust containing the spores of the causative fungus *Coccidioides immitis*. The possibility of infection through breaches of the skin is accepted although such an occurrence is regarded as very rare. The author describes the case of a 22-year-old negro soldier who cut his left index finger on a jagged can-edge while serving in the desert near Indio, California. An indurated swelling developed in the affected finger, and a sinus, connected with the bone, appeared and discharged a thin, ichorous pus containing pus cocci; but no fungus was noticed. A radiological examination showed destruction of the cortex and invasion of the medulla of the middle phalynx, with very little osseous regeneration, but no involvement of the epiphyseal ends of the bone. Sulphonamide treatment failed to give relief and the finger was amputated. Microscopic examination of the lesion showed a granuloma suggestive of tuberculosis, but in place of the tubercle bacillus there were numerous thick-walled spherules which did not show budding and were believed to be *C. immitis* [measurements of the spherules are not stated]. The coccidioidin skin test and the serum complement-fixation test both gave positive results and the diagnosis of coccidioidomycosis was considered to be confirmed. The infection, which appeared to be localized to the affected finger, is believed to have occurred through the wound caused by the can. *J. T. Duncan.*

DAVIS, H. V. & NEFF, F. C. **Histoplasmosis in Infancy.** *Amer. J. Dis. Children.* 1946, Feb., v. 71, No. 2, 171–7, 4 figs.

The authors have added two new cases to the growing record of infantile histoplasmosis. [See also IAMS, TENEN & FLANAGAN, this *Bulletin*, 1946, v. 43, 587.] The first case was a white female child who became ill at the age of 8 months with anaemia, fever, loss of weight and irritability, ending with emaciation and coma. There was evidence of bronchitis, the liver and spleen were enlarged and the lower extremities were oedematous. Blood examination showed 2,840,000 r.b.c., per cmm., haemoglobin 45 per cent., leucocytes 16,380 per cmm., of which 73 per cent. were lymphocytes (many immature forms) and 24 per cent. polymorphonuclears. The diagnosis made was "aleukemic leukemia", but at the autopsy *Histoplasma capsulatum* was found in the spleen, liver, myocardium, adrenals, lymph nodes, kidneys and lungs. The second case was a white, male infant, aged 4 months suffering from fever and cough with progressive loss of body weight and enlargement of the liver and spleen. Blood examination showed 2,950,000 r.b.c. per cmm., haemoglobin 51 per cent. with a normal leucocyte count. Histoplasmosis was suspected and this diagnosis was confirmed by finding *H. capsulatum* in sternal marrow smears and by culture of the fungus from the marrow and the blood. The histoplasmin skin

test gave a negative result, but a positive reaction was given by a similar test on the child's mother. The child died 72 days from the onset of illness and the diagnosis of histoplasmosis was confirmed at autopsy. *J. T. Duncan.*

CATANEI, A. Résultats de l'étude du pouvoir pathogène d'une souche soudanaise d'*Histoplasma capsulatum*. [**Results of the Study of the Pathogenicity of a Sudanese Strain of** *Histoplasma capsulatum*.] *Arch. Inst. Pasteur d'Algérie.* 1945, Dec., v. 23, No. 4, 260–68.

Using a strain of *Histoplasma capsulatum* isolated from localized histoplasmosis on the face of a male Sudanese described by CATANEI and KERVRAN [see this *Bulletin*, 1946, v. 43, 246], the author conducted a series of inoculation experiments on mice, guineapigs and rabbits. The materials used for inoculation were living cultures of the fungus [presumably in the mycelial form], and pus from lesions of experimental histoplasmosis produced in other animals by means of the same strain of *H. capsulatum*. The inoculations were made by the subcutaneous, intraperitoneal and intravenous or intracardiac routes. The rabbit was found to be wholly resistant to the infection, but the guineapig, when inoculated by the intracardiac route, developed lesions in the lungs from which the fungus was recovered in culture, and small granular lesions on the peritoneum following intraperitoneal inoculation. The white mouse was susceptible to infection by all three routes, but the lesions produced were less striking than those usually found in experimental histoplasmosis in this animal. In one of the mice the fungus was isolated in culture from the apparently healthy spleen two months after clinical recovery from the infection.

The author believes that the relatively low virulence of this strain of *H. capsulatum* explains the localized character of the disease in the human subject from whom it was isolated. *J. T. Duncan.*

HEAT STROKE AND ALLIED CONDITIONS.

KARK, W. **Urinary Symptoms of Heat-Stroke.** *South African Med. J.* 1946, Mar. 9, v. 20, No. 5, 111–13.

Frequency of micturition and oliguria have often been described in patients suffering from effects of heat. It is stated that in addition to these, dysuria, hesitancy, urgency, and suprapubic pain may also be present. These symptoms may be early and prominent, giving rise to a diagnosis of cystitis or stricture. There appears to be no fixed relation between the individual symptoms and the various types of effects of heat.

[The term "heat-stroke" is used here to cover all types of heat effects. No quantitative details are given of urinary output, or of the capacity of the bladder, measured at cystoscopy. Such measurements would be of interest, in view of the possibility that the frequent passage of small amounts of urine, so often noticed in the tropics, may be the result of shrinkage of the bladder—a kind of disuse atrophy. On the other hand, in true heat stroke, frequency is associated with polyuria, which may be caused by suppression of sweating and hydraemia. Oliguria in heat exhaustion is the result of dehydration, and is a valuable sign. The origin of the other urinary symptoms remains to be established.] *J. Waterlow.*

WRIGHT, D. O., REPPERT, L. B. & CUTTING, J. T. **Purpuric Manifestations of Heatstroke. Studies of Prothrombin and Platelets in Twelve Cases.** *Arch. Intern. Med.* 1946, Jan., v. 77, No. 1, 27–36.

Nine out of ten cases of heat stroke with temperatures of 110°F. or more showed petechial haemorrhages ; two others with temperatures of only 106°F. showed no petechiae [rectal temperatures are not specified but probably meant, as most of the patients were unconscious on admission]. All had dry skins. Four of the patients who had shown petechiae died, and at autopsy subendothelial and other internal purpuric manifestations were found ; one patient with no skin petechiae also came to autopsy, but he had petechial haemorrhages internally. All the severe cases when tested gave signs of diminished capillary tone. In all cases prothrombin time was estimated on admission, in eight of these it was increased to a greater or less extent ; when estimated later it was raised even more in all the cases investigated. Platelet counts were made on eight cases on admission ; in two only were counts over 100,000 obtained ; later counts were even lower. Evidence of hepatic failure was given by abnormal results of the hippuric acid test in three patients, and by actual necrosis of the liver in two of those who came to autopsy ; in four out of six cases in which it was estimated, the icteric index was raised. The authors conclude that the haemorrhagic manifestations of heat stroke are due first to a capillary dilatation which has become pathological with exposure to extreme environmental heat, and second to prothrombin deficiency secondary to hepatic damage. In those patients who survive the first few hours of the disease, therapy should be directed to the prevention of liver damage by administration of carbohydrates, vitamins, etc. ; but the authors warn against becoming " enthusiastic about the therapeutic correction of the prothrombin and/or platelet deficiency." Measures suggested are the exhibition of large doses, 50–60 mgm., of menadione parenterally (15 mgm. per day did not give dramatic results), and repeated transfusions of whole blood.

W. S. S. Ladell.

FAY, F. R. & SUSMAN, E. **On the Prickly Heat.** *Med. J. Australia.* 1945, Dec. 22, v. 2, No. 25, 453–6, 1 fig.

The authors describe a study of 46 officers serving in one of His Majesty's Australian ships during a prolonged naval action, lasting six days and nights, when their ship was within four degrees of the equator. Eighteen simple variable factors were analysed, and an attempt is made to postulate their effects on individual susceptibility to prickly heat. The subjects wore long-sleeved shirts, long trousers tucked into socks, boots, and, when necessary, anti-flash gear.

The average temperatures inside the ship were : dry bulb, 94°F., wet bulb, 81°F. ; the humidity was 57 per cent. A standard mixed diet was taken, and very little alcohol was consumed.

Of the 46 officers, 18 had prickly heat before the period of observation : during the period, eight more developed the eruption. The authors safeguard themselves from attack on statistical ground by stating that they appreciate that the number of individuals concerned was so small that the results are subject to the usual statistical fallacies ; with this proviso, their observations are summarized as follows :—

" (1) Factors which increase the liability of a person to prickly heat are : (*a*) age over thirty years, (*b*) fair skin, (*c*) ' highly strung ' type of mental make-up, (*d*) large salt intake, (*e*) working and sleeping below decks, (*f*) high temperatures of place of work, (*g*) long working hours, (*h*) battle dress or poorly ventilated clothing, and (*i*) perhaps the fact of belonging to blood group O (IV).

" (2) Factors which reduce the liability of a person to prickly heat are : (*a*) age below thirty years, (*b*) previous sun tan, (*c*) loose clothing, (*d*) open-air working and sleeping, (*e*) low temperatures of place of work, and (*f*) perhaps the fact of belonging to blood group A (II).

" (3) Factors having no effect on the incidence of prickly heat are : (*a*) weight, (*b*) sweat reaction, (*c*) wearing of open-necked shirts, and (*d*) the effects of the sun on the subject's skin.

" (4) Factors which from our investigations gave inconclusive results were : (*a*) type of work, (*b*) humidity, (*c*) brand of soap used.

" These various factors do not seem to be a cause in themselves, but when present they affect a susceptible person as indicated. The disease seems to be more constitutional than to be due to any one factor in particular."

[Besides the observations summarized above, the paper contains some clinical notes on the diagnosis and treatment of the conditions.]

R. M. B. MacKenna.

TROPICAL ULCER.

SHEPHERD, Margaret M. **Metastatic Osteomyelitis Secondary to Tropical Ulcer.** *Brit. J. Surgery.* 1946, Apr., v. 33, No. 132, 352–7, 5 figs.

In 11 out of 98 cases of tropical ulcer of the leg in young Gurkha soldiers, treated in hospital in Dehra Dun in the latter part of 1943, inflammatory lesions developed in various long bones ; the tibia was affected in six cases, the femur in 3, the fibula in one, the radius in one, and the clavicle was also involved in a patient in whom both tibiae were affected. The author has since seen two cases where the lesions were in the shaft of the humerus.

The first symptom was local pain and tenderness, not usually severe and not usually complained of for several days after its onset ; in seven cases there was slight fever. The time of onset of this complication was usually several weeks—4 to 27—after the ulcer appeared and the ulcer was then clean and healing except in one case.

" Radiologically the first change was a decalcification in the cortex of the diaphysis of a long bone. Then followed linear periosteal new bone deposit and a fluffy or woolly new bone having a broadly crenated outline. In some cases healing then occurred by deposition of calcium salts in the new bone. Very little resorption took place. In other cases changes indicative of osteomyelitis appeared before healing took place." The bone lesions are clearly shown in the radiographic illustrations.

Wassermann and Kahn tests were asked for and reports were received in nine cases, but in one the blood was haemolysed and in another it was contaminated ; the other seven were negative.

The bone lesions healed without special treatment (sulphathiazole was given in four cases) in from 5 to 27 weeks, average 12 weeks. In a footnote the author states that penicillin was tried in a few other similar cases with encouraging results.

[No bacteriological examinations appear to have been made except that in one case it is stated that blood culture was sterile.] *J. F. Corson.*

MANUWA, S. L. A. **An Excision Knife for Tropical Ulcers.** *Brit. Med. J.* 1946, Apr. 13, 574, 1 fig.

This knife is a bistoury curved on the flat. The author has found it useful for the excision of tropical ulcers.

MISCELLANEOUS DISEASES.

CULLINAN, E. R. **Medical Disorders in East Africa.** *Trans. Roy. Soc. Trop. Med. & Hyg.* 1946, Apr., v. 39, No. 5, 353–68, 1 map. [11 refs.] Discussion 368–72 [KEKWICK, A.; WILCOCKS, C.; MANSON-BAHR, P.; BIGGAM, A. G.; BOYD, J. S. K.; JAMES, S. P.; LOW, G. C.; MCCULLAGH, McK.; NAPIER, L. E.; CULLINAN, E. R. (in reply)].

This paper briefly surveys the medical disorders affecting British troops in the East Africa Command during the last 20 months of the recent war, and makes a plea for future co-ordinated clinical research in East Africa.

The East Africa Command covered over a million square miles, extending from 11°N. to 25°S. It included Kenya, Tanganyika, Northern Rhodesia, Nyasaland, Italian and British Somaliland, the reserved area of Abyssinia, Madagascar, Mauritius, the Seychelles and Zanzibar. The troops were fairly static, at the time, being in training for service in South-East Asia; and they comprised a cross-section of the fittest young adult native males of East Africa, and a representative sample of adult Europeans, all living under closely similar conditions.

The most prevalent medical causes of admission to Hospital, in both Europeans and non-Europeans, were malaria, dysentery and enteritis (including amoebiasis) and then upper respiratory infections. The incidence of other diseases, however, differed markedly in the two groups, dengue and typhus being found mostly among Europeans, while schistosomiasis, relapsing fever, leprosy and yaws were almost exclusively confined to the non-Europeans. Digestive disorders were nearly five times, skin diseases over three times, and psychoneurosis over twice as frequent among the Europeans as among the Africans. The killing diseases of the Africans were tuberculosis, meningitis and pneumonia, accounting respectively in 1944 for 16·0 per cent., 12·1 per cent. and 11·7 per cent., of all non-European deaths.

Nearly all the malaria in the mainland was due to *P. falciparum*, but in a few districts, especially in Somaliland, Madagascar and Mauritius, *P. vivax* was found, while in Mauritius, and rarely elsewhere, *P. malariae* occurred. The malaria season varied greatly from region to region, but in the hyperendemic areas transmission was "almost perennial". Immunity was labile, depending upon the frequency of infection, and while the disease among non-immunes was of all grades of severity, it was almost universally mild among the immune populations. It was therefore neither desirable nor necessary to give an immune African a full course of treatment for malaria.

Bacillary dysentery ran a mild course, with few exceptions, and the case-mortality was low; the deaths nearly all resulted from dehydration, which seemed to occur more rapidly among the Africans. In the treatment of the disease sulphapyridine seemed as effective as sulphaguanidine.

The incidence of amoebiasis rose among Europeans as the years of war went by, and in 1944 the number of European troops admitted to hospital with the disease corresponded to 20·27 per 1,000. Treatment followed conventional lines, with the usual rapid resolution of symptoms, but in many of the European patients the disease relapsed, and those with frequent recurrences were generally sent home to the United Kingdom.

Skin diseases were relatively uncommon in African troops, and among Europeans they were frequent only in humid stations. Tropical ulcers were very prevalent among the African troops in the earlier part of the war, but towards the end of the war had almost completely disappeared.

Psychoneurosis accounted for 17·59 per 1,000 of the admissions of the European troops to hospital, an incidence rate not unduly high in view of the prolonged absence from home, loneliness and lack of action. The majority of the European patients suffered from anxiety states, whereas hysteria was the common condition among the Africans.

Relapsing fever, common in many parts of East Africa, was largely confined to the native population ; it appeared to be tick-borne, except in Abyssinia, where the louse-borne type was also found. *Ornithodorus moubata* was the responsible tick vector. When the disease occurred in Europeans, cerebral complications appeared more frequently than among the Africans. Novarsenobillon seemed of little value in the treatment of the tick-borne fever, and, although penicillin had some effect, the results were not sufficiently good to justify its general use.

The incidence of schistosomiasis among Europeans was very small. The few Africans admitted to hospital with the condition gave no real measure of the true incidence of the infestation among the natives, as an examination of the urines of 1,408 African troops, all of whom were in active training and apparently fit, revealed that 13·56 per cent. were harbouring eggs of *S. haematobium*. The highest percentage of infected men came from Nyasaland, where there is a large lake whose surrounding population is considered by local observers to be heavily infected from early childhood, the infection rate being estimated at 90 per cent. of the inhabitants. Rectal schistosomiasis appeared to be relatively uncommon, and the incidence of *S. mansoni* throughout East Africa is not accurately known.

Acute pyogenic meningitis was much commoner in African than in European troops, and had a very severe clinical course ; usually the infection was meningococcal, but sometimes it was pneumococcal, no other local focus being found, and these pneumococcal infections were often particularly resistant to treatment, both with sulphonamides and with penicillin.

Dengue was particularly common in Diego Suarez, at the northern extremity of Madagascar, and 94·2 per cent. of all the cases in the Command occurred there during the first five months of 1944 ; Europeans were attacked over eight times as frequently as Africans. There were remarkable similarities between the clinical features of the disease and those of sandfly fever. There were a few small scattered outbreaks of idiopathic infective hepatitis ; the course of this disease was no more severe in Africans than in Europeans and the incidence was much less, while the opposite was true of " post-arsphenamine " jaundice, Africans being more frequently and more severely affected than Europeans. Acute anterior poliomyelitis was rare, excepting for a violent outbreak among the civilians in Mauritius early in 1945, when 1,000 cases occurred in a population of approximately 420,000, 95 per cent. of the patients being under the age of 10 years. Leprosy was not uncommon among African troops, and was almost always of the neural type. Although malnutrition was frequent in recruits, florid examples of nutritional deficiency were rare. There was, however, a sharp outbreak indistinguishable from beriberi among some East African troops stationed in Diego Suarez, whose diet for a time had consisted mainly of rice. This rice had been lightly milled, and in its uncooked state contained a theoretical sufficiency of thiamin. It was found, however, that while fresh lightly milled rice lost only 30 per cent. of thiamin in cooking, this rice, which was old and contaminated, lost over 70 per cent. and, moreover, it produced beriberi in pigeons.

Among young adult East African natives, pulmonary tuberculosis was generally acute and frequently ran a severe course with a high death rate. There is, however, a group with higher resistance which responds well to treatment, but unfortunately most of the patients are unwilling to stay in

hospital for longer than three months. The African refuses to be separated from his family, and one possible answer to the problem is the "settlement" system; a tuberculosis centre on the lower slopes of Mt. Kilimanjaro, in Tanganyika, is already doing excellent work in this direction.

The author stressed the need for co-ordinated epidemiological and clinical research in the Colonial Empire in the future, not only for its potential scientific value, but also for the interest it could give to large numbers of medical officers in remote stations. In June 1944, the D.D.M.S. inaugurated a Medical Investigation Committee for the purpose of encouraging, facilitating and correlating research by medical officers in the East African Command. The response was immediate and enthusiastic, and within a year a considerable amount of valuable work had been done.

In the subsequent discussion several speakers enlarged on the desirability of further and wider research in the tropics. Brigadier J. S. K. Boyd mentioned that a Colonial Medical Research Committee had been formed to foster research on a wide basis with whole-time research workers. C. Wilcocks thought that tuberculosis in the tropics demanded more attention, and stressed the importance of poverty and ignorance in the aetiology of this and many other diseases in the tropics. Colonel S. P. James was surprised to hear that nearly all the malaria had been due to *P. falciparum*, and suggested that other species of parasite were not without importance in East Africa. Dr. G. Carmichael Low stated that the diseases reviewed were much as he had seen them in East Africa more than 40 years ago, excepting that infection with *S. mansoni* was then common, as were other helminthic infestations, particularly filarial. Mr. McKim McCulloch remarked on the preponderance of appendicitis in Europeans as compared with Africans. *F. Murgatroyd.*

Avery, J. L. **Parasitic Infections among Natives of the Samarai District, Papua, New Guinea.** *J. Parasitology.* 1946, Feb., v. 32, No. 1, 25–9.

Stained thick blood films and faecal specimens (one of each from each person) of natives in New Guinea were examined for parasites; the faecal examination included a brine floatation method. One survey was made of a group of labourers, chiefly to ascertain filarial periodicity while another survey was made of "an entire native village: adults and children" [only three children, aged 0–4 years, had a blood examination in this village of 318 persons examined; all three had malarial parasites].

The following incidence of infection was found in the village: *P. vivax* 105; *P. malariae* 50; *P. falciparum* 7; *Wuchereria bancrofti* 97 (taken at 9 p.m. to midnight). No mepacrine was given to the natives except in the rare cases where seriously ill persons were taken to hospital. The microfilariae showed definite periodicity, increasing in the peripheral blood at night.

The incidence of *Entamoeba histolytica* was low—3 out of 53 labourers and 3 out of 300 villagers; other protozoa found were *E. coli, Endolimax nana, Giardia lamblia* [*G. intestinalis*], and *Trichomonas hominis* and all had a low incidence (1 or 2 per cent.).

Two species of intestinal helminths were found: *Trichuris trichiura* (1 out of 53 labourers and 126 out of 300 villagers) and hookworms (40 out of 53 labourers and 268 out of 300 villagers); the species of hookworm could not be determined.

Anopheles punctulatus punctulatus was very abundant; other mosquitoes present were *A. p. moluccensis* [*A. p. farauti*], *Aëdes scutellaris* and *Aëdes kochi.* *J. F. Corson.*

LINDSAY, S. F. **Fatigue Syndromes in West Africa.** *Brit. Med. J.* 1946, May 18, 758–60.

A number of men of the British Army in West Africa Command who showed signs of physical and mental fatigue were studied from the point of the relation of climate to ill-health in the moist tropics.

The cases, 86 in number, were classified into five groups, the first consisting of 64 with fatigue as the main symptom. This group was sub-divided into (1) those with signs of simple physical and mental fatigue, (2) those with exaggerated or abnormal psychological reactions, (3) those with toxic illness. The remaining groups consisted of those with psychoneurosis, depressive states, psychosis and a post-concussion syndrome, complicated by fatigue symptoms.

Investigation showed that the West African climate was only partly the cause of the breakdown. Everyone living in this climate is liable to experience some degree of languor, but most people learn to adapt themselves to the limitations thus put upon their activities. The part played by the climate is to aggravate any pre-existing weakness, physical or psychological. Even the problem of adjusting themselves to the ways of the African native is too difficult for some people and they react with irritability and frustration, leading to tiredness and depression.

The total personality with its physical, intellectual, emotional, social and moral components must be considered when studying reactions to climatic stress.

Some detailed case histories are given.

[An interesting study of fatigue problems in an unusual setting, providing some further confirmation of previous findings in various industrial environments particularly noticeable owing to the exaggerated conditions resulting from the war.] *May Smith.*

DOWLING, P. G. **Epidemic Polyarthritis.** *Med. J. Australia.* 1946, Feb. 23, v. 1, No. 8, 245–6.

This is a description of an outbreak of a short, mild fever accompanied by polyarthritis, which occurred among Australian troops in North Queensland during February, March and April, 1945. The disease was obviously the same as the "acute polyarthritis" described by HALLIDAY and HORAN as occurring in the Northern Territory of Australia [see this *Bulletin*, 1944, v. 41, 279]. An outbreak in Queensland in 1944 was described by SIBREE.

In the present outbreak 94 cases occurred among various units in a camp seven miles in length; in a unit at one end of the camp there were 47 cases; in four units a short distance away there were 39 cases; the remaining eight cases were from units in other parts of the camp.

Every patient suffered from pain and stiffness of several joints, especially those of the hands and feet; swelling was observed in about three-fourths of the cases, and there was effusion into one knee-joint in three cases.

The swelling, which was periarticular in most instances, persisted for four to seven days; the pain usually disappeared a few days later, but in three cases it lasted for three months. Some of the patients had no fever, but most of them had a slight rise of temperature to 99–101°F. for two to five days. One patient, exceptionally, had a temperature of 103°F. The onset was gradual. In 90 per cent. of the cases there was a papular or macular rash, which appeared on the first to the seventh day, and lasted for two to seven days; it was usually first seen on the trunk, then on the limbs; sometimes it was generalized. "In four cases small vesicles developed on the papules within twenty-four hours of the appearance of the rash, and these patients were first thought to

be suffering from varicella." Redness of the fauces was seen in 12 patients. One or more groups of lymph glands were swollen and tender in about half of the cases.

The leucocyte picture was normal. Blood cultures were sterile. The outbreak, like the others recorded, occurred in the "wet" season; it began two weeks after heavy falls of rain, and was associated with a great increase in the prevalence of mosquitoes. Two weeks after the commencement of the outbreak, and one week after starting mosquito-control measures, new admissions rapidly diminished in numbers.

Culex fatigans was the only mosquito of which adults were found in all the three camps in which a survey was made; it was present in large numbers. Larval *Aëdes notoscriptus* and *Aëdes alboannulatus* were found. Adult *Anopheles annulipes* were found in two of the camps, and adult *Culex lutzia halifax* in one. Other possible insect vectors were considered, but none was prevalent in the area at the time. There was no evidence of spread by contact, and the author concludes that "the possibility that this disease is a mosquito-borne infection requires investigation."

He suggests that the name "epidemic polyarthritis" is suitable for the condition, because it avoids confusion with other serious forms of polyarthritis.

[The name proposed by the author for this problem fever seems to be preferable to acute polyarthritis. As opportunities for investigation into the cause may not recur, the disease will perhaps remain one of the minor unsolved mysteries of the war. The name "polyarthritic febricula" would possibly have been more descriptive than the others suggested.] *John W. D. Megaw.*

RUDRA, M. N. & BHATTACHARYA, K. P. **Serum Phosphatase in Lathyrism.** *Lancet.* 1946, May 11, 688.

"Lathyrism is the result of degeneration of part of the nervous system" and there is "an intimate relationship between vitamin B_1 and the nervous system." The authors, therefore, studied the nutrition of lathyrism patients from this vitamin aspect, but found that the vitamin was present in normal limits in the blood and urine. They next estimated the serum-phosphatase in normal subjects and compared it with that of sufferers from lathyrism. In 12 of the former it ranged between 0·8 and 5·7 units, with a mean of 2·38; among 10 lathyrism cases it ranged between 18·7 and 56·5, with a mean of 38·7 units. It is suggested that this increase may destroy the circulating cocarboxylase, so that the patient is functionally, though not actually, deficient in vitamin B_1, with consequent affection of the nervous system.

This is put forward as a hypothesis, but the hiatuses to be filled are great. The authors can offer no explanation of the increase of serum-phosphatase in lathyrism and themselves make the suggestion that it may not be the cause, but the effect, of lathyrism, for, usually, the serum-phosphatase level is a measure of the severity of the disease. [A stimulating piece of work.]

H. Harold Scott.

GENERAL PROTOZOOLOGY.

LEHMANN, G. D. & PRENDIVILLE, J. T. **Occurrence of a Flagellate in the Sputum of a Case of Bronchiectasis.** *Brit. Med. J.* 1946, Feb. 2, 158–60, 2 diagrams. [17 refs.]

The paper describes a case of bronchiectasis in which flagellates, in diminishing numbers, were present in the sputum on four successive days. The disappearance of the flagellate coincided with the relief of symptoms under sulphapyridine treatment which, however, did not prevent a fatal issue. The

flagellate, 10–15μ in length by 5–7μ in breadth, was actively motile, its movements being the result of the action of two equal anterior flagella, and of amoeboid changes in shape. It was generally pear-shaped, the posterior broader end frequently being elongated to form a caudal process. In some respects the organism resembles the flagellate stage of *Dimastigamoeba gruberi* but this organism does not develop an elongated caudal process in its flagellate stage, which is merely transitory, the stable form being an amoeba. It is suggested that an amoeboid phase might have been present in the lung cavities and that the flagellate phase occurred only when dilution of the material with bronchial secretion and saliva took place. It seems not unlikely that the organism is an altered trichomonas, a possibility considered by the authors. No pathological significance is attributed to the presence of the flagellate in the material coughed up from the lung. The paper is illustrated by a number of line drawings. *C. M. Wenyon.*

CHIPPAUX, C. & CHIPPAUX-MATHIS, Jeanne. Le *Trichomonas vaginalis* chez la femme noire togolaise. Etude épidémiologique, clinique, pathogénique et thérapeutique. [*T. vaginalis* **in Togoland Women.**] *Méd. Trop.* Marseilles. 1944, Sept.–Oct.–Nov.–Dec., v. 4, No. 4, 269–300. [21 refs.]

The authors have examined 151 native women of Togoland, aged 18 to 45, for evidence of *Trichomonas vaginalis* infection which might account for the symptoms of pain and vaginitis of which they complained. Of these women 45 were found infected, giving an incidence of 29·8 per cent., which is nearly double the infection rate encountered among white women, making similar complaints, examined in Marseilles. The authors think that the higher incidence amongst the black women may be due to some particular racial susceptibility. They admit that *T. vaginalis* is usually present as a saprophytic organism only, but that occasionally it may take on pathogenic properties. The paper discusses many aspects of the subject, the authors basing their remarks on personal observations and a general review of the literature.

C. M. Wenyon.

GENERAL ENTOMOLOGY.

HUNTER, G. W., WELLER, T. H. & JAHNES, W. G., Jr. **An Outline for teaching Mosquito Stomach and Salivary Gland Dissection.** *Amer. J. Trop. Med.* 1946, Mar., v. 26, No. 2, 221–8, 13 figs. [17 refs.]

The technique of mosquito dissection described in this paper is not new, neither is the method of teaching it, but after trying many others they were adopted by the American Army Medical School as being the most satisfactory for the training of large groups of individuals who had no previous knowledge of entomology.

The course consists of one lecture on mosquito anatomy followed by two practical periods of two hours each. Uninfected mosquitoes are dissected during the first practical period and infected ones during the second. A full description of the technique is given, oöcysts and sporozoites are described and illustrated and there is a list of the necessary equipment. A useful paper for the beginner. *H. S. Leeson.*

SAUTET, J. & AUDIBERT, Y. Etudes biologiques et morphologiques sur certaines larves de moustiques en vue d'applications pratiques pour leur destruction. (Première partie.) [**Biological and Morphological Studies on Mosquito Larvae.**] *Bull. Soc. Path. Exot.* 1946, v. 39, Nos. 1/2, 43–61, 13 figs.

The work described in this paper was done at the Hygiene Research Centre, Marseilles, where the mosquitoes *Theobaldia longiareolata, Culex pipiens* and *Culex hortensis* are being studied.

An account of the structure and function of the terminal respiratory apparatus of the larva of *Culex pipiens* is followed by a description of some experiments on larvae imprisoned under water. Survival times of such larvae were recorded at different instars, in standing and running water, under winter, spring and summer conditions, in the presence and absence of aquatic vegetation and food. Usually six to eight larvae were put into two litres of water.

Some of the results are tabulated and briefly discussed, and, in general, tend to show that submerged larvae are able to withstand such conditions for longer periods in water which is cold and running than in warm, still water; the presence of food and aquatic vegetation helps to prolong their resistance. First and second stage larvae are shown to be more resistant to mechanical suffocation than are the older larvae.

The paper is to be continued. *H. S. Leeson.*

SIMMONS, S. W. & Staff. **Techniques and Apparatus used in Experimental Studies on DDT as an Insecticide for Mosquitoes.** *Supplement No. 186 to Pub. Health Rep.* Wash. 1945, 3–20, 11 figs.

Important outstanding problems in mosquito control by DDT are the number of mosquitoes leaving treated houses before having received a lethal dose of insecticide, and the relation between lethal effect and dosage, and interval since application, on different wall surfaces. The authors describe techniques used in investigating these subjects. This review merely indicates the general scope of their equipment, which is described in the original in sufficient detail to make exact reproduction possible.

Mortality amongst mosquitoes leaving treated houses is studied by means of a window-trap placed over windows on northern or western aspects of the house. Several types have been tried; in the most successful type some windows and doors were left open to allow free ingress of mosquitoes, and one or two windows are closed by means of a framework, in the general shape of a window, hinged at the bottom and opening outwards to an angle of about 15 degrees from the vertical. The upper horizontal surface of this frame has an opening over which a cage is placed and left for 24 hours, this is subsequently removed and used as a holding cage in which mosquitoes can be observed without further handling. A bigger catch is obtained by this means than by others which have controlled inlets as well as outlets, and specimens captured are considered to be a representative sample of those leaving the room by all apertures.

Testing of toxicity of surfaces may be needed under two sets of conditions: (1) in rooms which have been treated and occupied in a normal manner, and (2) in the laboratory where it is desired to remove all disturbing factors such as mechanical handling, so that the treated surface can be left under standardized conditions. For the first of these the authors use a holding cage in the shape of a truncated cone and made of plastic, a plunger cage resembling an enlarged syringe by means of which mosquitoes can be transferred with the minimum of trauma, and glass Petri dishes held in a special framework attached to the wall

by means of brackets, 15 to 20 mosquitoes being held between the Petri dish and the wall and preferring to alight on the latter as a result of their difficulty of holding on to the glass. After exposure to the treated surface, mosquitoes are liberated into holding cages for observation.

For laboratory tests the authors use a darkened holding cage, a glass lantern chimney which mosquitoes are persuaded to enter by light attraction, an air blast mechanism by which they are transferred without damage to the experimental cage, arranged to accommodate panels of wood or other material which have been treated under standardized conditions. At the end of the exposure time, mosquitoes are transferred to observation cages.

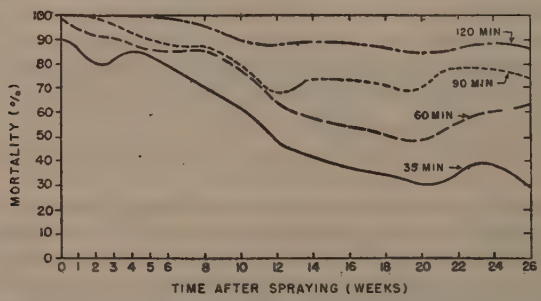
[These last two techniques provide a rapid method of accurately estimating the toxicity of surfaces to mosquitoes artificially held in contact with them, which should yield results which can safely be used in statistical comparisons. The same degree of reliability could not be attributed to the first technique for the estimation of mortality amongst mosquitoes entering treated rooms.]

G. Macdonald.

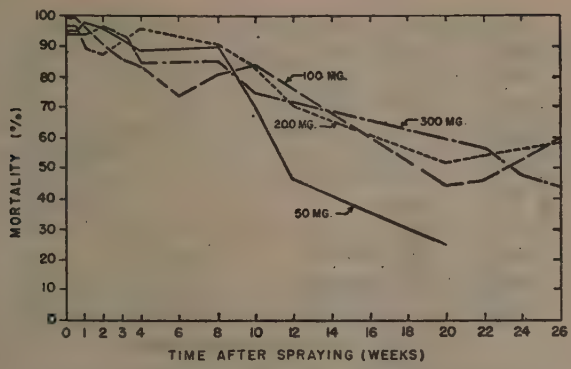
FAY, R. W., SIMMONS, S. W. & CLAPP, J. M. **Laboratory Investigations on the Toxicity of DDT Residues to Adults of** *Anopheles quadrimaculatus. Supplement No. 186 to Pub. Health Rep.* Wash. 1945, 21–34, 11 figs.

Using the technique described by SIMMONS and Staff (see above), *Anopheles quadrimaculatus* mosquitoes of both sexes as test insects, doses of DDT of 50, 100, 200, and 300 mgm. per sq. ft., exposure periods varying from 35 to 120 minutes, and periods of observation up to 26 weeks, the authors show that mortality varies directly with exposure time, but not materially with the dose of DDT applied, provided it is 100 mgm. per sq. ft. or more. In fresh films the effect of variations in the period of exposure of mosquitoes is relatively slight, but in older films it increases, until in films 26 weeks old there is a mortality of 31·2 per cent. amongst mosquitoes held in contact with them for 35 minutes and of 89·1 per cent. amongst those in contact for 120 minutes. These results are illustrated in the two graphs reproduced below.

The residual activity of DDT deposited from different solvents, again observed over a period of 26 weeks, showed moderate differences. The toxicity of a film deposited from an orthodichlorobenzene mixture wore off rapidly, and a Dreft-Talc mixture showed poor adhesion and had to be abandoned. Gas, condensate, kerosene, and "PD 544 C" and "PD 544 B" appeared to be better than others. Four different solvents were also used for the preparation



Average 48-hour mortalities of *A. quadrimaculatus* adults after 35-, 60-, 90-, and 120-minute exposures to DDT residue of 50 to 300 mg. per square foot from ½ to 26 weeks after application.



Per cent. mortalities of *A. quadrimaculatus* adults after 60-minute exposures to 50, 100, 200 and 300 mg. DDT per square foot residue at 1 to 26 weeks after application.

[Reproduced from *Supplement No. 186 to the Public Health Reports.*]

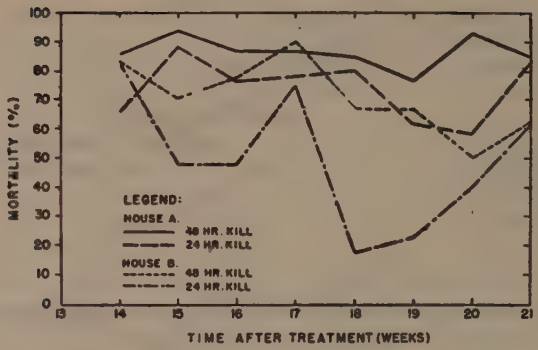
of films exposed to weathering, and no material difference was found between them. In each case direct sunlight produced a slow, steady deterioration in effect, whilst rain produced a rapid deterioration over the first four weeks, after which no further change occurred up to eight weeks.

[The observation that the dose of DDT does not materially affect mortality rates conflicts with the findings of other authors, notably METCALF *et al.* (this *Bulletin*, 1946, v. 43, 102). The range of doses in the two cases was very different, 50 to 300 mgm. in the present series, 40 to 1,000 in the previous series, but they do seem to display some material difference. The exact techniques used in the present series must be considered as making their results very reliable.] *G. Macdonald.*

TARZWELL, C. M. & STIERLI, H. **The Evaluation of DDT Residual Sprays for the Control of Anopheline Mosquitoes in Dwellings.** *Supplement No. 186 to Pub. Health Rep.* Wash. 1945, 35–48, 5 figs.

The "net mortality" of mosquitoes naturally entering unoccupied rooms was studied by the method elaborated by SIMMONS and STAFF [see above], in which a proportion of those attempting to leave are captured and held under observation for 24 or 48 hours. The majority of the mosquitoes were *Anopheles quadrimaculatus*, and about 77 per cent. of the dead recovered were males; this high proportion is attributed to the fact that the experiment was carried out close to breeding places, and possibly to a higher resistance of females than of males to DDT. The mortality figures obtained in treated houses were checked by the findings in untreated control houses, and corrected by a formula which took account of the numbers dying naturally in the untreated places. The results in two representative vacant buildings are shown graphically in Figure 1.

When a similar technique was tried in occupied houses the "net kill" was much lower. For periods of two to six weeks after treatment, mortalities of 39 per cent. at 24 hours and 54 per cent. at 48 hours were recorded, the reduction being attributed to the presence of furnishings, and objects hung on the walls, which greatly increased the amount of untreated surface on which mosquitoes might alight. There were indications that doses of 200 to 400 mgm. DDT per sq. ft. were more effective than doses of 100 mgm.



Effective 24- and 48-hour mortalities taken in window-traps of unoccupied houses A and B, treated with 200 mg. of DDT per square foot. Each point is a summation of 7 daily collections.

[Reproduced from *Supplement No. 186 to the Public Health Reports.*]

In addition to these trials on mosquitoes naturally entering rooms, others were made in which captured or insectary-bred *A. quadrimaculatus* were liberated into rooms, all openings from which could be occluded by traps, and which had been treated with 100, 200, 400, and 800 mgm. DDT per sq. ft. Five to 35 minutes after release the mosquitoes became irritated and began to move about, some towards the light, simultaneously suffering from tremors and incoordinated flight. The number moving towards the light gradually increased till the numbers resting on the untreated screen of the window trap reached a maximum between 30 and 60 minutes after release. Many of those moving towards the light had, however, already received a dose which proved fatal before they actually entered the window traps, and of those which entered them practically all died within 24 hours. Contrasting recently-applied and ageing films, it was found that with the latter the time required for knockdown was increased, but that otherwise the results were substantially the same as with the former. Rate of knockdown was also affected by dosage, 50 per cent. morbidity being reached at 93, 67, and 60 minutes after liberation into rooms treated with 100, 200, and 800 mgm. per sq. ft.

In some of the experiments the temperature was recorded, and it is stated that temperature greatly influenced the rate of knockdown, the higher the temperature the more rapid effect of the DDT. [In the opinion of the reviewer, the data presented are inadequate to substantiate this statement.]

G. Macdonald.

STIERLI, H., SIMMONS, S. W. & TARZWELL, C. M. **Operational Procedures and Equipment used in the Practical Application of DDT as a Residual House Spray.** *Supplement No. 186 to Pub. Health Rep.* Wash. 1945, 49–65, 5 figs.

Kerosene solutions of DDT were found to have practical disadvantages which made the use of emulsions preferable. A formula found useful for large scale work was :—DDT, 3 lb., xylene, 3 quarts, and Triton X-100 (a proprietary emulsifier) 6 fluid ounces. One gallon of a concentrate made to this formula, mixed with 6 gallons of water, makes a nominal 5 per cent. spray, of which 1 gallon to 946 sq. ft. gives a DDT dosage of 200 mgm. per sq. ft. In cold weather DDT is not so soluble, and the concentrate is, therefore, weaker ;

for winter work 2 lb. of DDT were dissolved in 1 gallon of xylene, with 0·2 quarts of Triton X-100, to form a concentrate of which 1 gallon, mixed with 3 gallons of water, gives a 5 per cent. emulsion.

For small scale projects, mixing was carried out in a 55-gallon wooden barrel mounted on rockers like those of a rocking chair, and fitted with handles by which it could be shaken ; by means of this, 50 gallons of concentrate could be mixed every hour. For work on a larger scale a power mixer was devised and is described in detail.

Both hand-operated and power sprayers were used. The hand sprayer was of the "pneumatic" type in which, before working, an air pressure of 50 lb. per sq. in. is developed by means of a hand pump. A nozzle giving a fan-shaped spray at a delivery of 0·2 gallon per minute was used, and was held 24 to 30 inches from the wall. The power sprayer, when adjusted to 60 lb. per sq. in. pressure, delivered 0·24 gallon per minute, with which delivery 230 sq. ft. could be treated every minute. Useful data are given on this, and accessory, equipment needed in practical work on the training of workers, the preparation of houses and the technique of spraying.

One overseer and two labourers using power equipment mounted on a truck could spray 40 houses per day, each averaging 1,750 sq. ft. of surface. The cost of treating 1,000 sq. ft. of surface was :—materials 35 cents, labour 24 cents, fuel, lubricants, maintenance and repair (by inference) 10 cents ; total, exclusive of overhead costs, 69 cents.

Piston-type atomizing hand sprays were found to be useless, and a power-operated paint sprayer was unsatisfactory. It was estimated that in urban areas a three-man crew with a power sprayer was equal to, or better than, a five-man crew with hand sprayers, and that the cost of their equipment was 400 dollars as against 200 dollars for the five men with hand sprayers.

G. Macdonald.

ARNOLD, E. H., FERGUSON, F. F. & UPHOLT, W. M. **The Experimental Use of DDT Sprays as Mosquito Larvicides.** *Supplement No. 186 to Pub. Health Rep.* Wash. 1945, 66–79, 8 figs.

Emulsions of DDT made from concentrates, consisting of 5 per cent. DDT in oil with various proprietary emsulsifier-spreaders, diluted [? 30 times] with water, gave 98 to 99 per cent. kill of anopheline and culicine larvae under a variety of conditions when the dose of DDT applied was 0·1 lb. per acre. There was, however, a disappointing lack of spread of the DDT from the point of application, and experiments showed that the lethal effect was limited to the distribution of the solvent ; consequently, emulsions were considered unsatisfactory for anti-larval work. Surface films of non-emulsified oil solutions were superior, and a 1·25 per cent. solution of DDT in No. 2 fuel oil with 0·5 per cent. B 1956 (a proprietary emsulsifier-spreader) was considered satisfactory.

A residual larvicidal effect was not obtained with small doses ; 0·5 lb. per acre gave control for only an additional week, and had the undesirable effect of killing fish. In one case, where 1·7 lb. per acre was applied to an area which had previously received 0·9 lb. per acre in divided doses, the water remained devoid of all animal life except plankton for over a month, and samples of the water showed definite toxicity to insectary-reared larvae.

Suspensions of DDT made by adding it to alcohol with a dispersing agent, and later diluting the mixture with water, had properties similar to those of emulsions. DDT dissolved in heavier-than-water oil, as a bottom application, was inferior to any of the surface applications as a larvicide, and was more lethal to other aquatic life.

An enquiry into the reason for the absence of residual larvicidal action showed that the bottom mud complex in some way binds the DDT in a form that is not available to larvae, though colorimetric estimation suggests that it is chemically unchanged; 100 gm. of mud will absorb as much as 4 mgm. of DDT in this way, and the effect is not dependent on bacterial action.

An experiment with minimal doses of DDT in fuel oil, and in gas condensate liquor, both of which produce surface films, showed that the latter was considerably the better vehicle, though with normal doses of 0·1 lb. per acre the two were equal in value. *G. Macdonald.*

LACKEY, J. B. & STEINLE, Mary L. **Effects of DDT upon some Aquatic Organisms, other than Insect Larvae.** *Supplement No. 186 to Pub. Health Rep.* Wash. 1945, 80–89.

DDT applied in a variety of vehicles with different emulsifiers has no effect on macroscopic vegetation, though it might be inactivated by the zoogleal coverings of plant stems. Doses of 1·0 part per million are poisonous to *Gambusia affinis*, which, however, avoids the treated area if there is a safe retreat, and thus may escape destruction. Water treated with this amount of DDT becomes non-toxic within 5 days of treatment. Tadpoles and crayfish are killed by similar doses, though with the latter the results are inconsistent. Aquatic worms and rotifers are not affected by doses of 0·25 to 1·0 part per million. *Daphnia* and perhaps other crustacea are killed in the laboratory by doses of 0·1 part per million, though *Clamydotheca* resist 20·0 parts per million. The evidence indicates that DDT as normally used is harmless to much, if not all, of the protozoal and algal population.

The authors suggest that the use of DDT might break the biological chain between protozoa and fish by eliminating aquatic insect larvae, small crustaceae, crayfish and fresh-water shrimps, and once this chain is broken it may take a long time to re-establish a normal fish population. They conclude that a detailed study of the subject should be made. *G. Macdonald.*

UPHOLT, W. M., GAINES, T. B., SIMMONS, S. W. & ARNOLD, E. H. **The Experimental Use of DDT in the Control of the Yellow Fever Mosquito** *Aëdes aegypti* **(L).** *Supplement No. 186 to Pub. Health Rep.* Wash. 1945, 90–96.

The fact that *Aëdes aegypti* breeds in water containers which do not contain mud (which inactivates DDT), or fish (which might be killed by large doses), might make it possible to achieve residual larvicidal action against this mosquito. Experiment shows this to be possible, and that the efficiency of anti-*Aëdes* campaigns can therefore be increased. A great variety of miscellaneous water containers were treated with DDT emulsion concentrates at doses of 1 part DDT per million and over. In all cases residual action was obtained, and in some for periods as long as six months. In many cases the containers had been emptied and refilled in the meantime and it seemed that the container itself remained toxic, despite the water changes, once it had been treated. This conclusion, arrived at in the field, was tested and verified in the laboratory, where it was shown that articles sprayed with DDT emulsion and subsequently repeatedly filled and emptied, remained toxic over several months. Similar results were secured when DDT was applied as a 20 per cent. mixture with a wettable powder.

Larvae of *Aëdes aegypti* " become morbid " as a result of exposure to DDT much more quickly than larvae of *Anopheles quadrimaculatus*, though they usually survive for a longer period of time. When final mortality is considered there is little difference in the resistance of the two mosquitoes.

The presence of DDT in water or on damp surfaces does not deter mosquitoes from ovipositing. *Aëdes aegypti* prefers to oviposit on moist surfaces rather than on water, but eggs laid on surfaces treated with DDT hatch normally, most of the larvae, however, die within three days of hatching. Pupae are not affected by DDT, though the vehicle in which it is applied may be lethal to them. *G. Macdonald.*

LINDQUIST, A. W., MADDEN, A. H., HUSMAN, C. N. & TRAVIS, B. V. **DDT dispersed from Airplanes for Control of Adult Mosquitoes.** *J. Econom. Entom.* 1945, Oct., v. 38, No. 5, 541–4, 2 figs.

This report describes the results of spraying 5 per cent. solutions and emulsions of DDT from a Piper Cub airplane over ground covered with dense mangrove and bush of varying density, for the destruction of adult *Aëdes taeniorhynchus* which were present in great numbers. The results were assessed by estimating the numbers of mosquitoes attempting to bite test subjects in the areas, before and after spraying, and in untreated neighbouring areas.

Twelve tests on plots ranging from 8 to 30 acres, each with 2 quarts of 5 per cent. DDT per acre, showed very similar results with emulsions and solutions. After spraying, observations were made at 1, 4, 7, 24, and in a couple of cases at 48 hours. At the first observation there was a reduction of about 60 per cent. and this increased at each subsequent count till at 24 hours the reduction varied from 69 to 99·5 per cent. and averaged 88 per cent. This gradual change, coupled with the dense vegetation which made direct contact of the falling spray with many mosquitoes unlikely, led the authors to believe that lethal action was largely the result of residual films on vegetation, and not an immediate effect of the spray.

Dusts containing DDT in similar quantities, and scattered from aircraft, caused no reduction observable at 24 hours. Two trials with smokes generated by injecting DDT solution into the exhaust pipe gave different results. In one no control was secured, in the other a 98 per cent. reduction was recorded at 24 hours. The authors believe that in this last case there had been poor smoke generation and most of the DDT had been liberated in a spray.

G. Macdonald.

LINDQUIST, A. & MCDUFFIE, W. C. **DDT-Oil Sprays applied from an Airplane to control** *Anopheles* **and** *Mansonia* **Mosquitoes.** *J. Econom. Entom.* 1945, Oct., v. 38, No. 5, 545–8.

In two tests carried out in the Panama Canal Zone, sprays containing 10 per cent. DDT in a mixture of cyclohexanone and oil were distributed from aircraft at doses of 2 quarts per acre, over mosquito-infested forest of moderate density. Before and after spraying, estimates were made of the numbers of mosquitoes, *Mansonia* spp. and *Anopheles* spp. mainly *A. albimanus*, attempting to bite test subjects. In each of the two areas there were six observation stations at each of which several counts were made. The averages of the results are shown below :—

First Test			Second Test		
Date	Mosquitoes per man per minute		Date	Mosquitoes per man per minute	
	Mansonia	*Anopheles*		*Mansonia*	*Anopheles*
Before spraying			Before spraying		
13/4	24	1	18/4	4·7	19
14/4	21	1·3	19/4	4	13
After spraying			After spraying		
15/4	0·18	0	20/4	0·19	0·37
16/4	0·46	0	21/4	0·58	0·45
19/4	0·64	0·025			
21/4	6·5	0·25			
6/5	22	1·12			

All larvae in a shallow lagoon, several acres in extent, were destroyed in the first test, and no fresh breeding was recorded for a week. *G. Macdonald.*

KIRK, R. & LEWIS, D. J. **Taxonomy of the Ethiopian Sandflies** (*Phlebotomus*). **I. Classification and Synonymy.** *Ann. Trop. Med. & Parasit.* 1946, Apr., v. 40, No. 1, 34–51. [29 refs.]

The literature on *Phlebotomus* is scattered, and the insects themselves are difficult to distinguish owing to their small size and to the fact that, recently, workers have used internal characters for the differentiation of species. Knowledge of the African species has tended to advance less rapidly than of those of the Oriental and Mediterranean regions. Kirk and Lewis's series of papers will therefore be very welcome.

The authors classify the Ethiopian sandflies into three sub-genera: *Phlebotomus* (restricted), *Sintonius* Nitzulescu and *Prophlebotomus* França & Parrot. The discussion of this classification, and of others that have been proposed, takes up the first six pages of the paper. The rest consists of a series of notes on the individual species, giving their synonymy, their broad distribution and some comments on the species themselves. No keys or other means for actual identification are provided, and consequently, pending the appearance of keys in further parts of the series, the present paper is not to be expected to provide a means for identification, though it does provide any worker on the sandflies with a mine of information that may save him from endless burrowing in the literature of the genus. *John Smart.*

DA CRUZ FERREIRA, F. S. A reacção das precipitinas aplicada aos dípteros do género *Phlebotomus*. [**Precipitin Reactions on** *Phlebotomus* **Species.**] *An. Inst. Med. Trop.* Lisbon. 1945, Dec., v. 2, 187–96. English summary.

YAO, Y. T. & WU, C. C. **Notes on the Chinese Species of the Genus** *Phlebotomus*. **Part VI. Sandflies in Chungking, Szechuan, with Description of a New Species,** *Phlebotomus koloshanensis*. *J. Parasitology.* 1946, Feb., v. 32, No. 1, 87–90, 8 figs. on 1 pl. [12 refs.]

PALMER, E. D. **Intestinal Cantharias due to** *Tenebrio molitor*. *J. Parasitology.* 1946, Feb., v. 32, No. 1, 54–5.

An infant whose food from the age of three weeks contained cereals began, at the age of 4 months, to vomit frequently between meals, and when 5 months

old began to pass by the rectum larvae identified as *Tenebrio molitor* (the meal worm); the adult beetles were later found in the infant's precooked cereal food. Several of these larvae were passed during 3 months, six were recovered and two of them lived for at least two weeks in a dry, air-tight jar. The child continued to gain weight but fed poorly, vomited frequently and had long spells of crying. There was no diarrhoea or melaena, and no larvae were vomited. Purges and enemas had no apparent effect, and larvae were still being passed 3 months after the first [see also this *Bulletin*, 1921, v. 17, 125; 1933, v. 30, 317]. *J. F. Corson.*

MICHENER, C. D. **A Method of rearing Chigger Mites** (*Acarina, Trombiculinae*). *Amer. J. Trop. Med.* 1946, Mar., v. 26, No. 2, 251–6, 4 figs.

As yet no really satisfactory method of rearing Trombiculid mites in the laboratory has been devised. It would be valuable to have some such technique for studies of the rickettsiae of scrub typhus carried by Trombiculid mites. This paper describes various techniques which may be useful to workers on this subject, but which have produced no notable advances in handling the mites. To obtain fully fed larvae an infested chicken or pigeon is placed in a cage above a dish of water, and the parasites which drop off after engorging are easily recovered from the surface of the liquid. They are removed from the surface on small pieces of newspaper; by this means they can easily be handled without damage. These larvae are then kept in a glass jar with a thin layer of plaster of paris covering its walls. This gives a suitable humidity without the production of moulds, and enables a high proportion of nymphs to be obtained.

The nymphs are kept in a similar jar in a mixture of five parts of sterilized soil with one part of chicken manure. This medium is exposed to the air so that the top surface becomes dry and the mites are discouraged from migrating from it. In about three weeks (at approximately 80°F.) some adults were produced, but a fairly high mortality was found and few laboratory-produced adults ever laid eggs.

Adult mites caught in the soil in nature readily laid eggs under similar conditions, and if the soil-manure mixture was kept firmly pressed the eggs were restricted to the surface layer and were easily found. They hatched to give larvae which could be fed on chickens; small pieces of wet paper were used to transfer the larvae to the host, and when these dried the mites walked on to the skin and attached themselves.

Although some success has been achieved here in breeding the mites, it is clear that many improvements of technique will be required before sufficient of these Trombiculid mites can be obtained for laboratory experiments.

Kenneth Mellanby.

WILLIAMS, R. W. **A Contribution to our Knowledge of the Bionomics of the Common North American Chigger,** *Eutrombicula alfreddugesi* **(Oudemans) with a Description of a Rapid Collecting Method.** *Amer. J. Trop. Med.* 1946, Mar., v. 26, No. 2, 243–50, 3 figs. [11 refs.]

The mite *Eutrombicula alfreddugesi* is a common cause of scrub itch in the southern part of the United States. The method described here for collecting large numbers of mites allows as many as 500 larvae to be obtained in one hour. About six white saucers are placed on the ground in likely areas, and the reddish coloured larvae are easily visible on the surface. They can be collected without damage by a simple aspirator similar to that used for catching mosquitoes, fleas, etc.

The author describes in detail the effect of the mite on the host. The production of the "histosiphon", and the area of necrosis produced by secretions of the larvae, are described in detail. As well as over-wintering as adults, these mites are shown to exist as fully fed larvae in the ears of rabbits, squirrels, etc., for long periods.

Some rather crude experiments are described. The larvae are said to be "negatively geotropic" and the rapidity of their movement (20 yards per hour) is said to compare (considering their relative sizes) with that of "a man travelling at 173 miles per hour for four hours." Bdellid mites are shown to be predators on this species of *Eutrombicula*. *Kenneth Mellanby.*

OLSON, T. A. & DAHMS, R. G. **Observations on the Tropical Rat Mite,** *Liponyssus bacoti*, **as an Ecto-Parasite of Laboratory Animals and Suggestions for its Control.** *J. Parasitology.* 1946, Feb., v. 32, No. 1, 56–60.

AULT, C. N. **Control of** *Boophilus australis* **in the Argentine by the Gamma Isomer of Hexachlorocyclohexane ("Gammexane").** [Correspondence.] *Nature.* 1946, May 25, 699–700.

LABORATORY PROCEDURES.

BOZICEVICH, J., HOYEM, Helen M. & WALSTON, V. M. **A Method of conducting the 50 percent Hemolysis End Point Complement-Fixation Test for Parasitic Diseases.** *Pub. Health Rep.* Wash. 1946, Apr. 12, v. 61, No. 15, 529–34.

In complement-fixation tests for helminthic and protozoal diseases, difficulties arise from the anti-complementary action of the complex antigens used; it is believed by the authors that most of the difficulties will be removed by the use of the technique described in this paper. It is similar in nature to the techniques of WADSWORTH [*Bulletin of Hygiene*, 1928, v. 3, 183], WADSWORTH, MALTANER and MALTANER [*ibid.*, 1939, v. 14, 132] and KENT, BUCANTZ and REIN (*J. Immunology*, 1946, v. 53, 37).

A standard haemoglobin solution is prepared by laking the centrifuged packed cells of a 2 per cent. sheep red cell suspension and adding a buffer solution, and from this a graduated colour standard is prepared daily as shown in the following table :—

TABLE 1.—*Preparation of colour standard.*

Percent. of hemolysis ...	0	10	20	30	40	50
Saline	0·80	0·80	0·80	0·80	0·80	0·80
Standard hemoglobin ...	0	0·02	0·04	0·06	0·08	0·10
2 percent. red cells ...	0·20	0·18	0·16	0·14	0·12	0·10

Percent. of hemolysis	60	70	80	90	100
Saline	0·80	0·80	0·80	0·80	0·80
Standard hemoglobin	0·12	0·14	0·16	0·18	0·20
2 percent. red cells	0·08	0·06	0·04	0·02	0

Fifty per cent. haemolysis is considered the most suitable for comparison. The haemolytic amboceptor and the complement are titrated at the same time, comparison being made with the colour standard; the optimum dilution of amboceptor is "that dilution beyond which further increase in the concentration of amboceptor does not appreciably change the quantity of complement required for 50 per cent. hemolysis." Once determined, it is used for the daily titration of complement and for sensitization of red cells in the tests. The unit of complement is that giving 50 per cent. hemolysis.

The test is arranged as shown in the following table :—

TABLE 4.—*The test proper*

Tube No. ...	1	2	3	4	5	6	7	8	9	10	11
Reagents											
Saline ...	—	—	0·30	0·25	0·20	0·30	0·25	0·20	0·30	0·25	0·20
Serum 1 : 5 ...	0·20	—	0·20	0·20	0·20	—	—	—	—	—	—
Serum 1 : 10...	—	0·20	—	—	—	0·20	0·20	0·20	—	—	—
Complement (4 units) ...	0·20	0·20	0·10	0·15	0·20	0·10	0·15	0·20	0·10	0·15	0·20
Antigen ...	0·20	0·20	—	—	—	—	—	—	0·20	0·20	0·20

The tubes are placed in the refrigerator at 5°C. overnight and next day 0·4 cc. of sensitized (15 minutes) sheep red cells is added to each tube and the tubes are placed in a water bath at 37°C. for 30 minutes, removed and read. Tubes containing 30, 50, 70 and 100 per cent. of red cells of the colour standard are removed and shaken well and compared with the tubes of the test; "any tube in the test matching the tube containing 30 per cent. cells or more is regarded as a positive, and any tube showing less than 30 per cent. fixation is regarded as negative."

J. F. Corson.

REPORTS, SURVEYS AND MISCELLANEOUS PAPERS.

HERMANS, E. H. De sterfte-statistiek der Nederlandsche Missionarissen. [**Mortality-Statistics of Dutch Missionaries.**] *Acta Leidensia* (*Scholae Med. Tropicae*). 1940–41, v. 15–16, 173–92. English summary (10 lines).

These statistics have been compiled for 40 years and are given for a very special population with due regard to age and sex distribution. Comparison is made with the mortality in Holland itself. During these 40 years 5,894 missionaries were sent out, 2,418 women, 3,476 men, of whom 604 died. The average age at departure was about 28 but the majority left at the age of 25 or 26 years. In Holland mortality from the 26th year up to and including the 35th year is about 30 per mille, which figure, for the mission field, rises to about 54 per mille. Much interest attaches to the main causes of death, which were malaria for East and West Africa and typhus for China. Death from all causes was of the order of 5·4 per cent. for missionaries in European missions and only 7·5 per cent. in the Netherlands Indies, but rose to as much as 18·8 per cent. and 17·3 per cent. in Oceana and China respectively. Several tables give the mortality figures in detail. Among the causes of the 32 violent deaths are listed sun stroke, scorpion sting, drowning, shipwreck and murder. This last cause was represented merely by a figure of 1 per 1,000 missionaries sent out. No deaths caused by wild animals or snakes were reported.

W. F. Harvey.

BOOK REVIEW.

ADRIAENS, L. [Docteur en Sciences chimiques, etc.]. **Contribution à l'étude de la toxicité du manioc au Congo Belge.** [Study of the Toxicity of Manioc in the Belgian Congo.] *Institut Royal Colonial Belge. Section des Sciences Naturelles et Médicales. Mémoires.* (Collection in —8°.) 1946, v. 13, No. 4, 140 pp., 2 diagrams.

This is an account of work carried out by the Chief of the Laboratory for Chemical Research in the Belgian Congo; it obtained Honourable Mention at the Annual Congress of the Belgian Royal Colonial Institute in 1940. The long delay in publication is no doubt due to the war.

Manioc, *Manihot utilissima*, Bitter Cassava, is used for its flour, for preparing tapioca, its starch, cassava cakes, etc., and it contains a "cyanogenetic principle," in common with *Phaseolus lunatus* and *Linum usitatissimum*, whereby, on addition of water, for example, hydrocyanic acid is set free and may cause fatal poisoning.

The author has undertaken an intensive study to determine the nature of the poison, the factors which participate in the elaboration of the cyanogenetic heterosides and how these may be destroyed or got rid of. He describes in detail the various ways in which the preparations of manioc are obtained, by maceration, by boiling, or by roasting; how, by repeated washing, by removal of the outer layers, or otherwise, the poisonous tuber can be made innocuous. These facts are already common knowledge and the author, after these preliminaries, goes on to describe his personal researches which have been directed to determining, first, the action of the emulsion of manioc on the amygdaloside, Congo manioc containing an emulsin which breaks down the amygdaloside, liberating the hydrocyanic acid. Secondly, the action of this emulsin on dimethylcyanhydrin, the synthetic aglucone of the heteroside of manioc; thirdly, the action of emulsin on the synthesis of aldehydes, ketones and glucides with HCN, using for this purpose benzoic aldehyde, acetone, glucose and certain glucidic products. Lastly, the action of decomposition products of aglycone on certain glucides. All these are considered and recorded with a wealth of detail, described in the letterpress and illustrated with a number of protocols.

The point of chief practical importance is a commercial one. Cassava or manioc is an excellent food, but unfortunately in its native state it is toxic. To remove the poison, at all events to reduce it to the smallest possible amount, careful preparation is necessary and if, in spite of all care, small quantities of the poison still remain, the addition of "proportionally insignificant" amounts of glucose will dispose of the danger. The method consists essentially in dividing the tuber (sometimes decorticated, but not always) into cubes or small pieces (*cossettes*), exposing them to the sun the whole day and at dusk placing them where they are protected from the moisture of the night air; next day the pieces are dried in a hot-air stove, at a temperature of 35–40°C., not higher than the latter, otherwise the product becomes brown and scorched-looking. If they are to be consumed at once, they should be cut small and left in a large quantity of water to soak; this water must be thrown away. For sale, the agents need the cossettes to be dry, really free from all moisture; to this end the drying should be rapid and the product protected from dew or the moisture of the night air; otherwise the drying process must be repeated; moreover, moisture will favour growth of mould and bacteria in transit.

This work will have much interest for the agricultural research chemist and, possibly, for the toxicologist, but makes no practical appeal to medical men.

H. Harold Scott.

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